AN ATLAS OF GENERAL AFFECTIONS OF THE SKELETON

BY

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TO MY COLLEAGUES
AND FRIENDS IN THE
MEDICAL PROFESSION

PREFACE

This book is compiled in the hope that it may be of assistance in the diagnosis of the various affections considered many of which are uncommon. For many years I have taken a special interest in affections of the skeleton that show multiple lesions an interest which has been stimulated by the kindly help and generosity of my colleagues and friends. It seemed to me a duty to make available to others some of the information to be gleaned from my collection of records a collection accumulated over a period of many years largely as a result of their generous help

The word Atlas in the title was suggested by the need for profuse illustration by numerous radiographs. The word General is not quite accurate since in many of the affections considered the skeletal lesions though multiple are not truly generalised. The essential criterion insisted upon has been that in every affection discussed more than one bone must be affected.

In the Introduction is given a classification of the various affections according to their etiology so far as this is known and this order has been followed with a few exceptions Because of certain similarities I thought it advantageous to consider some of them with affections of an entirely different etiology It seemed unnecessary to my purpose to discuss infective osteomyelitis among the conditions due to infection and toxaemia.

I have endeavoured to include what in my opinion are the chief facts of each condition. When known the cause of each is stated but no attempt has been made to discuss the various theories suggested when the etiology is obscure.

Though an extensive search of the literature has been made only a limited number of references has been attached to each chapter Whenever possible I have called attention to one or two articles which seem to me to comprise good resumés of the subject under discussion and to these I have added references to reports of unusual features or of complications of exceptional interest or importance Treatment has not been discussed.

I cannot sufficiently thank the many colleagues and friends who have supplied me with detailed records of cases under their care. My thanks are also due to the Editorial Committees of the British Journal of Surgery the British Journal of Radiology and the Royal Society of Medicine for permission to use illustrations already published in their Journals or Proceedings. Every effort has been made to acknowledge the source of individual cases referred to in this book. If I have omitted to acknowledge my indebtedness for any particular help I offer my humble apologies.

I am particularly indebted to the British Editorial Committee of the Journal of Bone and Joint Surgery in which some of the earlier chapters have been published, for agreeing to their inclusion here To their Editor Sir Reginald Watson-Jones I owe a special debt of gratitude for his courteous and skilful editing of those chapters. On many occasions I have been indebted to Dr L. M Hawksley for valuable advice on a pathological question. To my son I am very much indebted for reading the final proofs and for other assistance To Miss Bradbury it is impossible to express my gratitude adequately for her patient and tireless help but for her knowledge and amazing memory exerted on my behalf during the past many years my collection of records could never have been made or this volume compiled.

Finally I would like to express my thanks to Mr Macmillan and Mr Parker who on behalf of the Publishers have given me much expert co-operation and help.

H A Thomas Fairbank

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INTRODUCTION

The majority of the conditions and syndromes considered in this Atlas—some eighty in all—are well recognised as clinical entities. Some of the syndromes because of their rarity or for other reasons, have received only the briefest reference. The number of clinical pictures that have been described in the literature is endless and it has not been easy to decide whether or not to refer to a published syndrome. Some of the published cases are undoubtedly atypical examples of well known conditions in fact many have been published as such. For three of the titles used in this volume we have been responsible two of these appear to have met with a certain amount of approval. The various conditions with certain exceptions referred to below have been discussed in the order in which they appear in the following classification which is founded on the etiology so far as this is known.

TABLE I

CLASSIFICATION OF GENERAL AFFECTIONS OF THE SKELETON

Congenital Developmental Errors

Osteogenesis imperfecta.
 Osteogenesis imperfecta cystica.
Osteopetrosis.
Melorheostosis.
Diaphysial aclasis.
Dyschondroplasia.
 Maffucci s syndrome.
Metaphysial dysostosis (Jansen)
Familial metaphysial dysplasia.
Dysplasia epiphysialis multiplex.
Dysplasia epiphysialis punctata.
Osteopathia striata.
Osteopoikilosis.
Chondro-osteo-dystrophy
 (a) Morquio-Brailsford type
 (b) Gargoylism
Achondroplasia.
Ateleiosis (sexual)
Myositis ossificans progressiva.
Cranio-cleido-dysostosis.
Neurofibromatosis.
Arachnodactyly
Acrocephalo-syndactyly and allied conditions.
Engelmann s disease (?)

Acquired Affections of Unknown Origin.

Polyostotic fibrous dysplasia.
Leontiasis ossea.
Paget s disease
Senile osteoporosis

Due to Errors of Diet and Metabolism.

Infantile scurvy
Rickets (foetal, infantile resistant or continued and late or adolescent)
Coeliac rickets.
    Idiopathic steatorrhoea.
Osteomalacia.
Milkman's syndrome
Renal osteo-dystrophy (renal rickets)
Renal osteo-dystrophy in adults.
Fanconi's syndrome
Lipoid granulomatosis.
    Eosinophilic granuloma of bone
    Hand Schüller-Christian disease
    Letterer Siwe disease
    Gaucher's disease
Fluorosis.
Osteosclerosis due to bismuth, lead and phosphorus.
    Hypervitaminosis A
    Hypervitaminosis D

Due to Endocrine Errors.

Hyperpituitarism	Pituitary gigantism.
	Acromegaly
	Cushing's syndrome (may be due to fault in adrenal or thymu
Hypopituitarism	Pituitary dwarfism (asexual ateleiosis)
	Fröhlich's syndrome
	Progeria
	Simmonds disease

Cretinism
Infantile myxoedema (myxinfantilism)
Hyperthyroidism (thyrotoxic osteoporosis)
Hyperparathyroidism
Macrogenitosomia praecox.
Eunuchoid gigantism
Adreno-genital syndrome.

Due to Infection or Toxaemia.

Congenital syphilis.
Infantile cortical hyperostosis.
Hypertrophic osteoarthropathy
Cachetic infantilism

Due to Errors of Haemopoietic and Lymphatic Systems.

Leukaemia.
Hodgkin's disease (lymphadenoma)
Myelosclerosis.
Cooley's anaemia.
Multiple angiomata of bone

Multiple Neoplasms.

Skeletal metastases from carcinoma.
Myelomatosis.
Neuroblastoma.
Chloroma.
Lymphosarcoma.
Angio-endothelioma.
Sarcoma multiple primary or secondary

In the congenital group are included certain conditions in which the features are not necessarily obvious at birth though the developmental error leading to the particular dysplasia is undoubtedly congenital. A striking example is myositis ossificans progressiva, in which extra skeletal signs seldom appear for several years though they have been recognised occasionally as early as the first year of life and yet the diminutive big toes clearly indicate the congenital origin of the condition No attempt has been made to discuss the abstruse problem of genetic influences evidence is accumulating that other factors may play a part in the production of some of the congenital developmental errors. Of many of the conditions though recognised as entities for many years past the cause is still entirely unknown It seemed to us advantageous to consider in adjacent chapters certain affections of entirely different etiology either because a peculiar clinical feature is common to both or because the fundamental pathological change is the same in both. For instance hyperparathyroidism is considered after polyostotic fibrous dysplasia and leontiasis since fibrosis of the marrow is a prominent feature of the pathological changes in all of them. Eosinophilic granuloma is so closely allied pathologically to the lipoidoses that it is naturally considered with them Gargoylism though now regarded as due to a metabolic error and the Morquio-Brailsford type of osteo-chondro-dystrophy are dealt with in adjacent chapters because of some similarity in the vertebral changes. The two types of ateleiosis are considered together although the cause of only one is known. Hypervitaminosis A is briefly referred to after infantile cortical hyperostosis because of somewhat similar cortical changes in both. Senile osteoporosis the cause of which is uncertain is considered after the dietetic and metabolic errors Chloroma is briefly referred to with leukaemia since the blood changes are similar in both Lymphosarcoma and lymphadenoma (Hodgkin s disease) are naturally discussed together

There are still many cases met with which cannot be placed with confidence in any recognised group atypical achondroplasia is used not uncommonly and quite reasonably for the title of a published case. We must not expect every case of a particular affection to display the complete syndrome or clinical picture The changes may be more limited than usual and yet be typical of a well recognised condition They may be unilateral instead of general even when the cause is an endocrine error In certain affections this tendency is marked *e g* in dyschondroplasia and polyostotic fibrous dysplasia but even so the changes are seldom strictly unilateral. Among the conditions cited by Sternberg and Joseph (1942) as occasionally showing unilateral instead of bilateral changes are acromegaly and renal rickets In the last condition we have seen one wrist showing striking changes while the other was almost normal. We have also seen a woman with gross shortening of both humeri strongly suggestive of achondroplasia, while the whole of the rest of the skeleton including the skull was normal in every way If an unusual feature—unusual either because it is exceptionally well marked or is unique—is found in a case suffering from a familial affection this unusual feature will in all probability be seen in every member of the family who happens to be affected with the developmental error The same is true with regard to the absence of a feature which is usually present.

Certain general questions relating to bone pathology call for brief consideration We would refer the reader to the excellent account by Baker (1940) He insists on the difference

between *osteoporosis* and *hypocalcification* In osteoporosis e.g in hyperparathyroidism, there is increased absorption of bone de-ossification—not decalcification—occurs. Hypocalcification on the other hand implies a failure to calcify to a normal extent the bone matrix laid down and therefore there is an abnormal proportion of osteoid as is seen in rickets. Thirdly the density of the skeleton may also be subnormal as a result of *deficient formation of bone matrix* as occurs in osteogenesis imperfecta. Most authors however use the words osteoporosis decalcification, or rarefaction to denote subnormal density of the bones regardless of the pathology If one separates the cases showing general, or at least widespread, lack of bone density in radiographs into three groups osteoporosis is present in hyperthyroidism and possibly also in renal osteodystrophy in adults in addition to hyperparathyroidism In hypervitaminosis D osteoporosis may occur coupled with hypercalcaemia and metastatic calcification in the soft tissues (Baker 1950) Hypocalcification occurs in coeliac rickets idiopathic steatorrhoea and osteomalacia, as well as in ordinary rickets. Lastly deficient formation of matrix occurs in infantile scurvy renal rickets Fanconi's syndrome senile osteoporosis Cushing's syndrome and almost certainly in the general atrophy resulting from prolonged cachexia and recumbency as well as in osteogenesis imperfecta. Subnormal density of uncertain pathology is seen in Simmonds disease

It is rather surprising how vague and misleading are many of the medical text books including some on pathology on the nature of osteoid many leave the reader with the impression that osteoid is nothing but uncalcified bone matrix and some even say so definitely yet what we were taught many years ago is still correct namely that osteoid may certainly be partially calcified. There is no doubt that bone matrix may be hypocalcified, but it cannot be hypercalcified.

The removal of bone is now regarded as always due to the activity of osteoclasts even *in the presence of inflammation or new growth. The hypothesis of solution of the lime salts* without destruction of the matrix (halisteresis) receives little support nowadays.

The theory that bone atrophy from disuse is merely the result of relative hyperaemia (Watson-Jones and Roberts 1934) has never entirely appealed to us. The relative absence of stresses and strains which normally promote bone formation seems a much more likely cause We still however await an explanation of the occasional occurrence of the patchy type of atrophy producing mottling that may quite strongly suggest malignant infiltration of the bone It is seen in adults more often than in younger patients, and most frequently we believe as the result of complete immobilisation of a limb for a fracture. The correct diagnosis may be a matter of considerable importance Harris (1933) pointed out that in atrophy the transverse trabeculae suffer before the longitudinal so that an atrophic metaphysis may show a finely striated appearance In our experience this atrophic metaphyseal striation is much more frequently seen in children than in adults In this connection we may note that longitudinal striation may be seen occasionally in coeliac rickets and idiopathic steatorrhoea, as well as in the condition for which we have suggested the title of osteopathia striata. Striation both longitudinal and transverse may be seen in the clubbed metaphyses of osteopetrosis when the X rays are sufficiently hard Striation of a much coarser type and limited to a few bones may be produced by the columns of unossified cartilage in dyschondroplasia and by the streaks of dense fibrosed bone seen in some cases of polyostotic fibrous dysplasia and of neurofibromatosis.

The *increased density* of a mass of dead cancellous tissue is still commonly regarded as only apparent and due entirely to contrast with the atrophic bone around. That this is incorrect is readily proved by comparing the density of the affected bone e.g the head of a femur with the corresponding bone on the other side in a patient whose general activity precludes the possibility of disuse atrophy being present on the sound side. Collapse and compression of the dead bone are accepted by some as partly responsible but these certainly cannot account for all the abnormal density In the early stages of pseudocoxalgia the head

of the femur may show no signs of collapse or only slight flattening of the convexity and yet the whole head may be denser than its fellow with complete loss of the fine cancellous structure which should be visible in a film What can account for this except the deposition of calcareous matter in the marrow spaces? We know of no convincing proof of this in aseptic necrosis but we have twice seen dead cancellous bone that was definitely chalky like a tubercular sequestrum in the presence of purulent infection the astragalus was affected in both cases partially in one and completely in the other In one of these Dr L. M Hawksley in a section specially made without decalcification proved the presence of a calcareous deposit in the cancellous spaces (Fairbank 1939) We know of no sections having been made of aseptic necrosis of the femoral head without preliminary decalcification

Just as decreased density is the result of diminution in the amount of normally calcified bone so increased density of living bone is usually due to increase in the number and thickness of the trabeculae and only occasionally is it further increased by a deposit of calcium in the marrow spaces or by masses of calcified cartilage such as may be seen in osteopetrosis. Calcium spheroids may add to the density in leontiasis ossea and in Paget s disease (Eden 1939) Abnormal density may also be caused by an ossifying or calcifying tumour

The following Table shows the amount of calcium inorganic phosphorus and phosphatase usually found in the blood in various conditions.

TABLE II

BLOOD CHEMISTRY IN VARIOUS AFFECTIONS OF THE SKELETON

Affection	Serum Calcium	Plasma Phosphorus	Alkaline Phosphatase
Osteogenesis imperfecta	+ or −	−	+ slightly
Osteopetrosis	N or + (especially if calcinosis present)	N or −	N
Osteopoikilosis	N	N	N
Myositis ossificans progressiva	N	N	N
Engelmann s disease	N	N	+ (in one case)
Polyostotic fibrous dysplasia	N or + (slightly in a few cases)	N	+ (often not always)
Leontiasis	N	N	+ (sometimes)
Hyperparathyroidism	+ (markedly)	−	+ if bones affected)
Paget s disease	N	N or + (often)	+ (markedly)
Scurvy	N	N	− (always)
Rickets	N or −	− or N	+ (varies with activity of disease)
Coeliac rickets	− (often)	N or −	+ (usually)
Idiopathic steatorrhoea	−	N or + or −	+ (certainly if fracture present)
Osteomalacia	− or N	−	+
Renal rickets	− (rarely +)	+	+ (sometimes)
Renal osteodystrophy of adults	N or + or −	+ (markedly)	(+ slightly)

N = within normal limits + = increased − = diminished.

TABLE II (Continued)

BLOOD CHEMISTRY IN VARIOUS AFFECTIONS OF THE SKELETON

Affection	Serum Calcium	Plasma Phosphorus	Alkaline Phosphatase
Fanconi syndrome	Slightly + or N	–	+ (slightly)
Senile osteoporosis	N	N	N
Lipoid granulomatosis	N	N	N
Cretinism	N	N	– (markedly)
Thyrotoxic osteoporosis	N	N	+
Congenital syphilis	N	N	N
Infantile cortical hyperostosis	N	N	+ (in some cases)
Hodgkin's disease	N	N	+
Skeletal metastases Osteolytic	N or + (if decalcification is rapid)	N or – (if cachexia) or + (if renal insufficiency)	+ (often, especially if osteoplastic)
Osteoplastic	– (slightly)	N	
Prostatic metastases	N	N	+
Myelomatosis	+ (sometimes)	N or + (slightly)	N or + (slightly)

N = within normal limits + = increased – = diminished.

Acid phosphatase is always markedly increased when prostatic metastases are present. Exceptionally in Paget's disease there may be a slight increase.

Marked hypercalcaemia is of great importance in the diagnosis of hyperparathyroidism since apart from this it is present only in myelomatosis and very occasionally in widespread carcinomatosis. References has already been made to hypercalcaemia in hypervitaminosis D a very uncommon condition. Alkaline phosphatase in the plasma, it will be noted, is raised in all conditions in which there is hypocalcification or osteoporosis as well as in some in which hyperplastic changes predominate. Senile osteoporosis is an exception; in this the fault lies in the failure to form bone matrix, not in its calcification, and the plasma phosphatase is normal in amount. It is increased temporarily by a fracture, irrespective of the nature of the general skeletal affection that is present. As a help in diagnosis alkaline phosphatase estimations are disappointing and are practically useless. The amount may, however, be a guide to the activity of rickets and indicate response to treatment. It is diminished in amount, be it noted, only in two conditions, in scurvy and to a marked degree in cretinism. Acid phosphatase estimations, on the other hand, may be of great importance when metastases from prostatic carcinoma are suspected, since if sufficiently increased no other diagnosis is possible. The only other condition in which, occasionally, it is somewhat raised is Paget's disease.

In the hope that they may be helpful in the diagnosis of a difficult case we have prepared lists of the various conditions in which certain outstanding features are encountered. We may suitably begin with *dwarfism* (Table III) which forms part of the clinical picture of so many of the affections we are about to consider. By dwarfism is meant a reduction in stature below what is considered the lowest limit for a normal individual of a given age. Infantilism, on the other hand, implies the undue retention of childish characteristics, mental, sexual and physical; skeletal retardation forms part of the clinical picture, in spite of the fact that the epiphyses may be late in fusing, if indeed they fuse at all. Dwarfism may be the result of diminished growth of the bones or of deformities, or of a combination of the two. The centres

for the epiphyses may appear late and the rate of growth be retarded the epiphyses fusing late as in cretinism and coeliac rickets On the other hand the epiphyses may fuse early causing premature cessation of growth in female children affected by hyperactivity of either the ovaries or the adrenals, initial skeletal precocity is followed by premature fusion of the epiphyses the early tendency to gigantism ending in some degree of permanent dwarfism Premature fusion may also occur in some cases of achondroplasia. Dwarfism may be the chief feature of a case or no more than one sign perhaps the least important of a particular abnormal condition

The whole skeleton may be affected to an approximately equal extent as in many cases of osteogenesis imperfecta in which deformities following fractures are only partly responsible for the subnormal stature. But in several conditions the dwarfism is more marked in the limbs than in the trunk, producing the short limb type familiar in achondroplasiacs. On the other hand the trunk may be more affected than the limbs as in both types of chondro-osteo-dystrophy and also in cases with marked deformity of the spine resulting from caries or other causes. Dwarfism may be confined to one limb or affect the arm and leg of one side only Dyschondroplasia is the commonest cause of unilateral dwarfism and may produce gross irregularity in the length of the limbs in one lad of eighteen years the affected leg was ten inches shorter than the other (see page 70)

TABLE III

DWARFISM

General.

- Osteogenesis imperfecta (excluding severe pre-natal cases)
- Diaphysial aclasis.
- Osteopetrosis.
- Progeria.
- Cachectic infantilism.
- Congenital syphilis.
- Macrogenitosomia praecox.
- Adreno-genital syndrome
- Burnier s Syndrome.
- Laurence-Moon syndrome.

Short Limb Type.

- Osteogenesis imperfecta (severe pre-natal cases)
- Dysplasia epiphysialis multiplex.
- Dysplasia epiphysialis punctata.
- Achondroplasia.
- Rickets.
- Coeliac rickets and idiopathic steatorrhoea.
- Renal rickets.
- Pituitary dwarfism (asexual ateleiosis)
- Ateleiosis (sexual)
- Fröhlich s syndrome
- Simmonds disease
- Cretinism.

Short Trunk Type

- Chondro-osteo-dystrophy (Morquio-Brailsford)
- Gargoylism
- Spinal caries.
- Severe scoliosis (including some congenital cases)

A mild degree of dwarfism may occur in Gaucher's disease and in idiopathic steatorrhoea when the onset is sufficiently early it is also included in a few unnamed syndromes of which only isolated cases have been reported.

There are two chief types of excessive growth of the skeleton or gigantism, both due to endocrine errors. Pituitary gigantism results when the hyper secretion becomes effective during childhood or adolescence many of these giants become acromegalic later The other form of gigantism is the eunuchoid type due to hypogonadism in this the epiphyses may appear late fusion is invariably delayed, genital infantilism is present and the limbs are disproportionately long

In several of the affections the ulna is noticeably shorter than the radius when this occurs the lower ends of these two bones are often turned towards each other A *short ulna* has been seen in diaphysial aclasis dyschondroplasia, Morquio-Brailsford type of chondro-osteo-dystrophy gargoylism achondroplasia and in a condition which Brailsford (1944) calls peripheral dysostosis. The fibula is unduly short much less frequently in achondroplasia the fibula is often less stunted than the other long bones and may be decidedly longer than the tibia

Another curious deformity met with in children is *angular kyphosis* not due to caries in the dorso-lumbar region, with one vertebral body reduced in size and slightly displaced backwards. This is seen typically in many cases of the Morquio-Brailsford type of chondro-osteo-dystrophy and, more consistently in gargoylism. A similar deformity has been found in s me cases of cretinism neurofibromatosis and achondroplasia, and also in otherwise apparently normal babies (Kemp 1950) In our experience and we have seen this deformity in all these conditions it is much more suggestive of the abnormality seen in gargoylism than that met with in the Morquio-Brailsford affection.

Increased density affecting more than one bone is a prominent radiographic feature in a large number of the affections discussed in this volume (Table IV) The extent of the involvement of an individual bone and the number of bones affected varies enormously in the more severe cases of osteopetrosis practically every bone in the body may be almost uniformly and completely dense including the epiphyses. Areas of increased and decreased density may occur together in a case either in the same bone as in Paget's disease or in different bones It should be remembered that more than one bone may be affected by chronic osteomyelitis leading to sclerosis.

TABLE IV

INCREASED DENSITY
(affecting more than one bone)

Lines of arrested growth	Paget's disease
Osteopetrosis	Fluorosis.
Melorheostosis	Bands due to lead phosphorus and bismuth.
Dysplasia epiphysialis punctata (shafts only in some cases)	Cretinism.
Osteopoikilosis	Infantile cortical hyperostosis.
Neurofibromatosis	Hodgkin's disease.
Englemann disease	Myelosclerosis.
Polyostotic fibrous dysplasia	Skeletal metastases (particularly breast and prostate)
Leontiasis ossea	

Increased den [illegible] *rtebral bodies* without signs of collapse the density often being remark [illegible] produced by Paget's disease metastases from prostatic or mamm [illegible] H [illegible] kin's disease and leukaemia the lower dorsal and

lumbar bodies are those usually affected. When the whole spine is involved th necessarily to the extent that each body is completely dense either osteopetrosis o is responsible Very occasionally leontiasis of the skull may be accompanied by incre density of one or two of the upper cervical vertebrae.

Curious *dense patches in the metaphyses* of some of the major long bones irregular in shape but sometimes roughly triangular usually transgressing the epiphysial line and often extending into the epiphysis have been met with occasionally in young patients suffering from one of the general affections of the skeleton We have seen these most frequently in the bones about the knee and at the lower end of the tibia in osteogenesis imperfecta Some indication of this feature was seen in one child as young as two years. In a girl of fourteen years the abnormal density in the femur and tibia near the knee joint consisted of masses of dense rings (see Fig 23) We have seen these dense patches also in the Morquio-Brailsford type of chondro-osteo-dystrophy coeliac rickets renal rickets (slight) and in polyostotic fibrous dysplasia. They formed a striking feature in two published cases of adolescent scurvy (see Figs. 320 and 330) These opaque patches of course differ markedly from the transverse dense lines or bands seen at the ends of the metaphyses in cretinism, and in poisoning by lead, phosphorus and bismuth and from the healing line in rickets and also from the dense lattice " between the clear zone and the epiphysial disc in scurvy and congenital syphilis. In the milder cases of osteopetrosis the phalanges which in this condition are usually less affected than the rest of the skeleton, commonly show a definite band of increased density abutting on the epiphysial lines.

A limited amount of increased density due to crushing may be seen in the spine as the result of *collapse of one or more vertebral bodies* the causes of which we have listed in Table V

TABLE V

COLLAPSE OF ONE OR MORE VERTEBRAL BODIES

Trauma.	Metastases from carcinoma.
Spinal caries.	Myelomatosis.
Osteomalacia.	Angioma.
Senile osteoporosis.	

Also occasionally in

Eosinophilic granuloma	Aleukaemic leukaemia.
Hand Schüller-Christian disease.	Ewing s tumour
Gaucher s disease.	Osteoclastoma.
Hodgkin s disease.	Cushing s syndrome (osteoporosis)
Paget s disease	

The affections below the line in this list are much less commonly the cause of vertebral collapse than those above the line but collapse has been seen or reported, at least once in all of them. In most cases the collapse is most marked in, if not entirely confined to the anterior part of the body But more or less uniform reduction in depth of the whole body usually associated with increased density and producing an appearance distinctly suggestive of Calvé s disease of the spine has been reported in eosinophilic granuloma Hand Schüller Christian disease and Gaucher s disease all members of the lipoid granulomatous group There seems to be little doubt that vertebra plana, as it is now commonly called is an exceptional feature met with in these and possibly also in other affections rather than a clinical entity

Shallow vertebral bodies throughout most or the whole of the spine constitute an important feature of the Morquio-Brailsford affection and are seen in a *mild form in*

osteogenesis imperfecta. In both these conditions the bodies are spread as well as reduced in vertical measurement. Two cases diagnosed as dysplasia epiphysialis multiplex had shallow vertebrae. In conditions such as rickets which produce general reduction in density of the bone in children, and also in osteomalacia and senile osteoporosis, the vertebral bodies are relatively shallow and their upper and lower surfaces are concave while the discs are relatively wide and biconvex; these changes occur with no sign of crushing, though this may be seen in ad... in the adult cases in whom more than one body in the lower part of the spine are tr... affected.

Irregular ossification of several epiphyses may be seen in dysplasia epiphysialis multiplex and punctata, cretinism, dyschondroplasia, osteopoikilosis and in both types of chondro-osteo-dystrophy. In some cases of osteopetrosis, a condition that may be subject to remissions and intermissions, the centre of an epiphysis may be denser than the more recently formed bone around it, or the centre may be relatively clear and surrounded by a dense ring, which is surrounded again by a clearer zone. The carpal and tarsal bones may show similar changes; in one case of osteopetrosis the os calcis showed no less than five narrow dense bands separated by less dense bone. When skeletal growth has been arrested, *e.g.*, in scurvy, a ring of increased density surrounding a translucent centre may be seen in an epiphysis. When the femoral head is the only epiphysis affected, besides the well known additional causes of irregularity in its shape and density, namely pseudo-coxalgia, arthritis of all kinds, Charcot's disease and caisson disease, it is worth remembering that a femoral head frequently shows gross changes in Gaucher's disease.

Among the clinical features common to several conditions are *limitation of movement* and flexion deformities of some of the major joints, particularly the elbows, knees and shoulders. Limitation of some joints and laxity of others may be found in the same case. Limitation may be seen in dysplasia epiphysialis multiplex, is common in the punctata variety, and is also present in achondroplasia, hypertrophic osteoarthropathy, myositis ossificans progressiva and (confined to the affected limb) in melorheostosis. In Léri's pleonosteosis the wrists and fingers are particularly affected. In acrocephalo-syndactyly actual ankylosis of some major joints may be found. In gargoylism limitation of joint movement is often severe and widespread, particularly in the upper limb. In the Morquio-Brailsford type both limitation and excessive laxity may occur, even in the same patient. In arachnodactyly also both occur, but hypermobility is more common than contractures.

Cutaneous abnormalities may occur in association with several of the more or less widespread bone affections. They have been seen in the following: melorheostosis (scleroderma), dysplasia epiphysialis punctata (thickening of skin, adherent skin in palm, calcification), osteopoikilosis (dermato-fibrosis lenticularis disseminata), neurofibromatosis (pigmented spots and fibromata), Albright's syndrome and Gaucher's disease (pigmentation), scurvy (ecchymoses), Hand-Schüller-Christian disease (yellow pigmentation and papular eruptions), Cushing's syndrome (purplish abdominal striae), asexual ateleiosis (pigmentation of face), Werner's syndrome (dermatosis and trophic ulcers), leukaemia (petechiae) and Hodgkin's disease (lesions and pigmentation).

In acromegaly thickening of the skin of the hands, feet, face and scalp, with clubbing of the fingers, occurs; somewhat similar changes may be seen in hypertrophic osteoarthropathy, the skin thickening being particularly marked above the wrists and ankles in the idiopathic familial variety.

In Maffucci's syndrome, in which both the enchondromata of dyschondroplasia and cavernous angiomata are present, the angiomata are essentially subcutaneous or deeper, but many are visible even when the skin itself is not involved.

The following is a list of *affections of the eyes* which occur in association with bone dysplasias. Optic atrophy occurs in osteopetrosis, leontiasis, Paget's disease, neuroblastoma, gargoylism, acromegaly and acrocephalo-syndactyly. In one reported case optic atrophy

complicated dyschondroplasia. Congenital cataract is conspicuously common in dysplasia epiphysialis punctata, corneal opacities and nystagmus in gargoylism dislocation of the lens tremulous irides and small myotic pupils in arachnodactyly retinitis pigmentosa in Laurence Moon syndrome pingueculae in Gaucher's disease xerophthalmia in coeliac disease and in China but not apparently in this country cataract in osteomalacia. Optic neuritis occasionally occurs in Fröhlich's syndrome and also in addition to interstitial keratitis in congenital syphilis. In acromegaly various ocular palsies may develop and opacities of the lens in idiopathic steatorrhoea.

Asymmetry of the face which may occur early and be responsible for the patient seeking advice has been seen in leontiasis ossea, both when this occurs alone and when it forms part of polyostotic fibrous dysplasia, dyschondroplasia, infantile cortical hyperostosis acromegaly and also secondary to facial palsy in osteopetrosis

Symmetrical enlargement of the lower thirds or more of the femora with loss of the normal trumpet shape is seen in Gaucher's disease familial metaphysial dysplasia and osteopetrosis (in which there is frequently clubbing of the metaphyses of the major long bones) Enlargement and distortion of the lower femoral shaft but without the same tendency for the changes to be bilateral and symmetrical are seen in diaphysial aclasis dyschondroplasia and in leukaemia. More or less similar metaphysial distortion will be found in some of the other bones in these conditions except in Gaucher's disease in which this change is confined to the lower ends of the femora.

Indentation of the pelvis is common and occurs in a number of conditions. It has been observed in osteogenesis imperfecta rickets (including the resistant and late types) coeliac rickets idiopathic steatorrhoea, osteomalacia, renal rickets Albright's syndrome hyper parathyroidism Paget's disease and pelvic metastases from carcinoma and also of course as the result of trauma and in cases of protrusio acetabuli.

Separation of epiphyses either true separation or the result of a metaphysial fracture may occur in congenital syphilis scurvy renal rickets and in the hips only in Fröhlich's syndrome It is also seen occasionally in hyperparathyroidism provided that the onset is sufficiently early

Unlike the short big toes seen in myositis ossificans progressiva, abnormally *long big toes* do not appear to have any diagnostic significance We have seen bilateral enlargement occurring in individual cases of the Morquio-Brailsford type of chondro-osteo-dystrophy arachnodactyly pituitary gigantism and eunuchoid gigantism enlargement of one big toe only occurred in an atypical achondroplasiac and in one case with no other developmental error except coxa vara

In Table VI we have enumerated the conditions in which more or less spontaneous *multiple fractures* either partial or complete are seen Appended to the list are the affections in which the appearance of some of the fractures has occasionally justified a diagnosis of Milkman's syndrome.

TABLE VI

MULTIPLE FRACTURES
(more or less spontaneous)

Osteogenesis imperfecta.	Osteomalacia.	Paget's disease
Severe rickets.	Renal rickets.	Fanconi's syndrome
Coeliac rickets	Polyostotic fibrous dysplasia.	Hyperthyroidism
Idiopathic steatorrhoea.	Hyperparathyroidism.	Senile osteoporosis (spine)

MILKMAN'S SYNDROME

Osteomalacia	Coeliac rickets.
Severe rickets (including the resistant and late types)	Idiopathic steatorrhoea.

Finally we return to the pathological side of these general affections of the skeleton a consider those in which fibrosis occurs the marrow spaces being occupied to a varying exte by cellular fibrous tissue We have arranged the affections in groups according to the m distribution of the fibrosis. In some it is the outstanding feature of the histology whil others it is of secondary importance or occurs only in the later stages of the bone lesions.

Fibrosis of the marrow is widespread but not universal, in hyperparathyroidism re rickets (some cases) renal osteodystrophy of adults osteomalacia myelosclerosis and so cases of osteogenesis imperfecta and osteopetrosis. It is found in the metaphyses, occupy space which should be filled by newly formed bone and normal marrow in scurvy re rickets and congenital syphilis. Local replacement of bone by fibrotic lesions occurs polyostotic fibrous dysplasia and in some cases of neurofibromatosis. Fibrosis accompar by new bone formation is seen in Paget s disease leontiasis ossea and some cases of polyost fibrous dysplasia and neurofibromatosis fibrosis has also been found, but only in a few ca in the dense lesions of melorheostosis and in infantile cortical hyperostosis and Engelman disease. In Paget s disease the fibrous tissue is less dense and more myxomatous-look than that found in most cases of osteofibrosis and it is often extremely vascular La fibrosis may occur as a late secondary change in the bone lesions of Hand-Schüller-Christ disease and Gaucher s disease and occasionally in leukaemia ending finally in osteosclero

In spite of having a mass of facts available for reference the diagnosis of an atyp case may be an extremely difficult problem. There will always be a few cases which we only allocate to the collection of unique and at present unclassified conditions. It is har necessary to stress the importance of complete clinical and laboratory investigations e when the diagnosis of a case seems to be obvious. Not only will mistakes be thus occasion avoided, but a mass of detailed information as to incidence and pathology will be accumula which may eventually lead to the discovery of the causes of some of the more obscure affectio In many of the well recognised conditions discussed in this volume we are completely help so far as specific treatment is concerned.

The tendency nowadays to resort to a complete radiological survey of the skelet particularly when a lesion of uncertain nature has been discovered in a bone has proved immense diagnostic value and has brought to light many interesting cases. When the chan are widespread the first step towards making a diagnosis should consist in determining th anatomical localisation we should ask ourselves whether the chief changes are confined the shafts the metaphyses or the epiphyses or whether they are more or less generalised the affected bones.

Tomography is proving useful occasionally in demonstrating with greater accuracy extent of the pathological changes, notably in affections of the spine

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CHAPTER 1

OSTEOGENESIS IMPERFECTA
and
Osteogenesis Imperfecta Cystica

Osteogenesis imperfecta (synonyms fragilitas ossium idiopathic osteopsathyrosis periosteal dysplasia) is characterised by fragility of skeletal bones. The cause is unknown. Cases may be grouped as pre-natal and post-natal but there is no clear-cut distinction between the two groups except in the date of the first fracture which depends upon the severity of the disorder Pre-natal cases are on the average decidedly more severe many die at birth or survive only a few days or weeks. The exact proportion of surviving to fatal cases is unknown. A child may sometimes survive several months despite birth fractures of many ribs. Osteogenesis imperfecta tarda is the term often applied when there is delay in occurrence of the first fracture for example, a girl with intensely blue sclerotics sustained the first of many fractures at the age of seven

Hereditary and familial influences are apparent in a minority of both groups but more often in the post-natal group The disorder may be inherited through either parent Many family trees have been published some covering four generations with certain members marked as having blue sclerotics some also with bone fragility but others without (50 per cent, Fraser 1934)

Sex—Both sexes are affected females more frequently than males of thirty five cases known to the writer nineteen were females.

Blue sclerotics fairly deep indigo and not just blue as may often be seen in normal babies, may be present in both groups of cases but more frequently in the post-natal group The depth of colour sometimes fades with age

Otosclerosis may occur in those who live till the third decade but deafness has twice been reported as early as the thirteenth year (Cleminson 1926 and Bigler 1923) Bickel *et al* (1943) analysing a series of forty patients found deafness in 45·5 per cent. of the hereditary and only in 17 3 per cent of the non-hereditary cases. Of adults with blue sclerotics 60 per cent. are said to develop otosclerosis with or without evidence of bone fragility (Rodger 1930) Osseous fragility blue sclerotics, and deafness constitute Van der Hoeve's syndrome. *Laxity of joints* with susceptibility to strain and dislocation is not uncommon in families afflicted with one or more elements of the syndrome.

Osteomalacia—An osteomalacic element (mollities) *i.e* softening leading to bending, may be present in addition to fragility of bone and thus contributes to the development of deformities, particularly in pre-natal cases This feature is strikingly displayed in the pelvis which is indented and tri radiate in 25 per cent. of all patients.

Fractures—The number of fractures varies enormously In severe cases fractures are spontaneous and cause little if any pain. A newly born child may exhibit as many as 100 fractures many involving the ribs. One patient with rather less severe manifestation of the disorder but nevertheless of the pre-natal type and with blue sclerotics died at the age of eight having sustained ninety-eight fractures. One bone is often fractured repeatedly for example a child sustained twenty three fractures of only three bones. Refracture may of course be favoured by the additional osteoporosis which results from immobilisation of the first fracture or by persistent angulation of the fragments or by both these factors.

Dwarfing—Most severe cases are dwarfed. Dwarfing is accentuated or indeed largely accounted f r by deformities of the limbs and curvature of the spine Scoliosis is often severe and is present in at least a quarter of the cases. In pre-natal cases the limbs may be relatively short sometimes to a striking degree

Skull—The typical skull is broad, with prominent parietal and occipital bones (*crâne à rebord*) the ears are directed downwards as well as outwards. In some familial and hereditary cases the skull has prominent frontal and occipital regions with no bulge or ridge in the temporal region.
Teeth—The milk teeth are poorly calcified and semi-translucent or waxy The permanent teeth are better calcified even in post-natal cases, and they are usually normal in appearance.
Intelligence is at least up to the average.
The musculature is extremely feeble in all but milder cases, this hypotonicity being no doubt secondary to fractures and deformities.
Blood chemistry varies but is usually within normal limits, and is of no diagnostic value.

Clinical progress—A tendency towards improvement is often evident. This is seen most frequently in mild pre-natal and in post-natal cases. A few patients in spite of severity of the disorder survive for many years for example a boy a pre-natal case was alive at the age of nineteen though bedridden since birth. Another pre-natal case only slightly less severe and markedly dwarfed is still able to earn her living as a secretary at the age of twenty nine

Pathology—The essential pathology is imperfect formation and imperfect calcification of bone trabeculae. Islands of cartilage are seen, notably under the periosteum, with chondroid or incompletely calcified osteoid trabeculae taking the place of properly calcified bone. The periosteum is thickened, and there is failure to form a normal shell of cortical bone beneath it. The bone is discontinuous and fragmentary The medullary contents may be in part fibroid, lymphoid, or fatty Deficiency in numbers of osteoblasts has been stressed as an essential factor (Knaggs 1924) but histological study of nine cases has shown great variation. In some the number of osteoblasts was quite numerous although the formation of bone was deficient.

Radiographic appearances—*Three groups of cases may be defined*
Type 1—Thick bone type (Fairbank 1927 1930)—These are severe pre-natal cases, born with limbs which are stunted as in achondroplasia and with numerous fractures notably in the ribs. The major long bones are short they are usually broad and thick, and show one or more fractures with ample callus. The proximal segments of the limbs the femora and humeri, are most severely affected, but the tibiae may also be enlarged. The appearance of the bones suggests that the thickening is not due entirely to callus formation following recent or remote fractures. It may be seen up to three months after birth but is seldom met with later Other bones show general osteoporosis and are similar to those seen in Type 2.
Type 2—Slender fragile bone type—This condition is seen in pre-natal cases which survive more than a few months and in all post natal cases. The skeleton as a whole is osteoporotic and the long bones are usually slender The cortex is characteristically thin and of deficient density The extremities of the bone often appear large and in older children they may show varying degrees of honeycombing Occasionally the shafts of some long bones, perhaps after repeated fracture, may be slender and yet surprisingly dense as compared with the ends of the bones. Deformities due to fracture or bending are common. Transverse lines of dense bone straight or wavy often mark the ends of the metaphyses. In one ante-natal case, at the age of fourteen years many rings of dense bone were seen in the epiphysial lines in the region of the knee joint. The fibulae may be reduced to little more than faint lines. The skull is thin and Wormian bones may be present. The pituitary fossa is normal. The petrous bone may show excessive density The vertebral bodies are translucent shallow spread and biconcave the intervertebral discs being biconvex.
Type 3—Osteogenesis imperfecta cystica—This name was suggested in 1935 for cases with pronounced honeycombing of bones. It is extremely rare. Only two living patients and one post mortem skeleton are included in this series. Th dates from birth. It is definitely progressive Cystic changes which are more in the lower than in the

upper limbs become increasingly evident with advancing years. During the first few years of life the upper limbs may show no more than simple osteoporosis. Deformity due to fracture and bending of bone is progressive. Hereditary and familial influences are not in evidence. In the two cases here recorded the sclerotics were not blue. The condition differs from multiple diffuse fibrosis of bone in that bone change occurs much earlier the radiographic appearances are not really similar and the histological appearances are quite different.

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CASE 1—OSTEOGENESIS IMPERFECTA—Thick Bone Type—Pre-natal

(Figs. 1 to 4) Male. Lived three days. Third child—others healthy No history of bone fragility in family Ossification of skull very imperfect and patchy Very large fontanelle Bossing of parietal bones. Numerous fractures including most of the ribs (under Dr G F Still)



Fig 1

Case 1—Greatly thickened cylindrical femora with multiple fractures the thickening is not entirely due to callus Upper ends of tibiae somewhat enlarged.



Fig. 2

Case 1—Note that there are fractures of all long bones including the clavicles which show some relati thickening also fractures of most of the ribs



Fig. 3

Case 1—Not the relativ shortness of limbs suggesting chondr oplasia

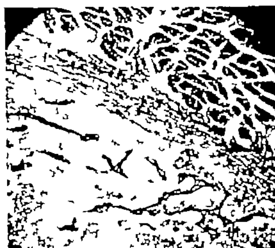


Fig. 4

Case 1— ect n of femoral shaft. Fragmentary bone format n complete absence of continuous wtic l la er beneath thickened periosteum in this case marked deficiency of osteoblasts

CASE 2—OSTEOGENESIS IMPERFECTA—Thick Bone Type—Pre-natal

(Figs. 5 and 6) Female. Lived ten weeks. Seventh child Mother very poorly nourished during pregnancy Other children healthy Skull very imperfectly ossified. Serum calcium low—5·45 mg per cent. (Under Dr F J Poynton)



Fig 5

Case 2—Note the short thickened humerus with fracture and callus formation The radius and ulna are not generally thickened, but are poorly calcified with thin translucent cortices and somewhat bulbous extremities



Fig 6

Case —The tibiae as well as the femora are affected by the general thickening which is apparently not due to callus.



FIG 2

Case 1—Note that there are fractures of all long bones including the clavicles which show some relative thickening also fractures of most of the ribs.



FIG. 3

Case 1—Note the relative shortness of limbs suggesting achondroplasia.

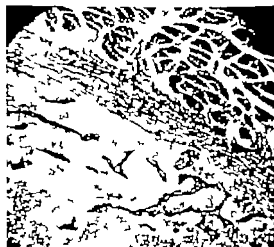


FIG 4

Case 1— ection of femoral shaft Fragmentary bone formation compl te absence of continuous cortical layer beneath thickened periosteum in this case ma ked deficiency of osteoblasts

CASE 2—OSTEOGENESIS IMPERFECTA—Thick Bone Type—Pre-natal

(Figs. 5 and 6) Female Lived ten weeks. Seventh child Mother very poorly nourished during pregnancy Other children healthy Skull very imperfectly ossified. Serum calcium low—5·45 mg per cent. (Under Dr F J Poynton.)



FIG. 5

Case 2—Note the short, thickened humerus with fracture and callus formation The radius and ulna are not generally thickened but are poorly calcified with thin translucent cortices and somewhat bulbous extremities



FIG. 6

Case 2—The tibiae as well as the femora are affected by the general thickening which is apparently not due to callus.

CASE 3—OSTEOGENESIS IMPERFECTA—Slender Bone Type

(Figs. 7 and 8) Girl aged six years. History imperfect but almost certainly pre-natal in origin. Only child. Dwarfed. Has had many fractures. Sclerotics blue but not markedly so.



FIG 7

Case 3—Femora show very slender shafts with much deformity due mostly to malunion of fractures. Typical osteoporosis of the ends of the bones and the epiphyses. Pelvis slightly deformed.



FIG.

Case 3—Typical ... ctly ossified tibia ... arked
due more to bend... an to fractures. ... n
Not the poor co... ones which do ... n
... ency is due to

CASE 4—OSTEOGENESIS IMPERFECTA—Ante-natal (Brother of Case 5)

(Figs. 9 and 10) First fracture at six months though disease certainly ante-natal. Severe case. Has never walked though aged eleven years when last seen. Sclerotics not noticeably blue. Elder sister also affected (Case 5) but a brother and sister, the first and third children of the family, are normal. No known hereditary influence. Died when aged nineteen years.



Fig. 9

Case 4—Tibia when aged 5 years (Fig. 9) shows extremely slender fragile bones with one fracture. When aged 8½ years (Fig. 10) extremities of femur show typically poor ossification. Central portion of shaft, slender but sclerosed. Ununited fracture with persistent tendency to angulation.



Fig. 10

CASE 5—OSTEOGENESIS IMPERFECTA—Ante-natal (Sister of Case 4)



Fig. 11

Case 5 at 1 years of age—Slender femora with coxa vara. Tri-radiate pelvis and scoliosis. Shaft of left femur fractured.

CASE 5—OSTEOGENESIS IMPERFECTA—Ante natal (Sister of Case 4)

(Figs. 11 to 13.) Born with fractured humerus. First seen at age twelve years. Sclerotics not blue. Has shown some tendency towards improvement. Angular deformity of right tibia and left femur resulted in very delayed union of fractures of these bones with a strong tendency to refracture. Was able to walk with appliances for various periods between fractures. Dwarfed—not entirely by fractures. Severe scoliosis. Tri-radiate pelvis—bones are therefore soft as well as fragile. At age twenty-nine years is able to walk and work as a secretary.



Fig. 12

Case 5 at 16 years of age—Note the slenderness of right femur and marked shortening of left femur due mostly to anterior bowing.



Fig. 13

Case 5 at 19 years of age—Left femur shows gross anterior bowing the result of repeated fractures, one incompletely united after many months.

CASE 6—OSTEOGENESIS IMPERFECTA

Ante-natal (Fig 14) Male aged seventeen years Born with one leg fractured. History of at least seventeen fractures. Sclerotics markedly blue Half-sister (same mother) has blue sclerotics but no fragility Tri-radiate pelvis Scoliosis.

CASE 7—OSTEOGENESIS IMPERFECTA

Post natal (Fig 15) One of twin girls aged seven years Both were affected and both showed blue sclerotics The onset was post-natal. There were familial and hereditary factors. A comparatively mild case



Fig 14

Case 6—Note the unusual general cancellous appearance with poorly defined cortex and general osteoporosis The deformity suggests bending of the bones rather than malunion of fractures but the leg has been fractured at least once

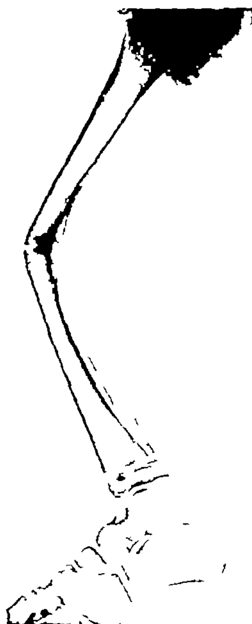


Fig 15

Case 7—This leg has been fractured nine times the last a year ago Shows typical slender fragile type of bones with imperfectly united fractures very easily refractured. Child was walking Deformity corrected by open operation

CASE 8—OSTEOGENESIS IMPERFECTA—Ante-natal

(Figs. 16 and 17.) Female baby aged nine months. Born two months prematurely with a leg broken. The head was markedly flattened antero-posteriorly. A very severe case with multiple fractures of nearly all ribs, both thighs, both legs, both arms and both forearms, and with gross deformities of the limbs.

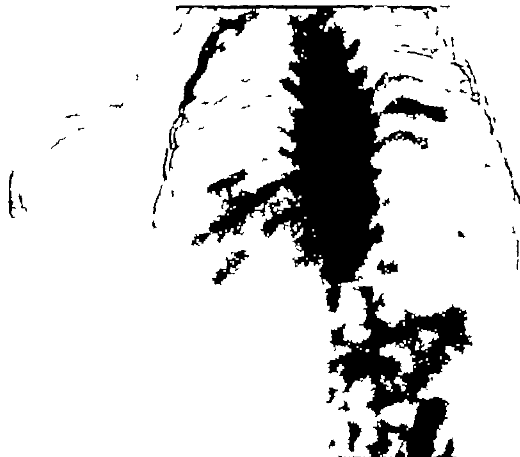


Fig. 16

Case 8—Note that nearly all the ribs are fractured; some are broken in two or three places. Nevertheless the child was alive nine months after birth. The upper limb is typical of the condition, with multiple fractures and gross deformity.



Fig. 17

Case 8—Severe ante-natal case (aged nine months) with multiple fractures of many ribs (Fig. 16) and of all four limbs (Fig. 17). Exceptionally marked fragility with gross deformity of all long bones of the lower limbs.

CASE 9—OSTEOGENESIS IMPERFECTA—Mild Post natal Case

(Fig 18) Male aged seven years. The patient s father broke his leg three times between the ages of fourteen and sixteen but has not blue sclerotics. No other fractures in family The child s sclerotics are rather blue. Only three fractures to date.



Fig 18

Case 9—Spine shows osteoporosis with very shallow biconcave vertebral bodies and deep biconvex discs.

CASE 10—OSTEOGENESIS IMPERFECTA

(Figs. 10 to 22.) Male aged nine years. Very numerous fractures dating from birth. Scoliosis and tri-radiate pelvis. Circumference of head twenty two and a half inches—of abdomen twenty three inches. Has never walked. Sclerotics not blue. When sitting height was seventeen inches. Blood chemistry shows no striking abnormality. Was still alive at the age of nineteen years. (Under Mr Tyrrell-Gray.)



FIG. 19

Case 10—Note the absence of cortex and the suggestion of honeycombing of the bones



FIG. 20

Case 10—The bones are grossly deformed and there is almost complete absence of cortex.



Fig. 21

Case 10—Radiographs of lower limbs shows gross deformity with irregular density both the result—at least in part—of multiple fractures.



Fig. 22

Case 10—Male aged 9 years with very numerous fractures dating from birth. Note the characteristic bulge in the temporal regions. The circumference of the head was twenty two and a half inches, the circumference of the abdomen twenty three inches, the sitting height seventeen inches. Calcification of the teeth is not bad.

CASE 11—OSTEOGENESIS IMPERFECTA

(Fig 23) Girl aged fourteen years. Pre natal onset No hereditary or familial influence Temporary teeth were markedly translucent Sclerotics not blue Many fractures had been sustained—fourteen in the first three years of life

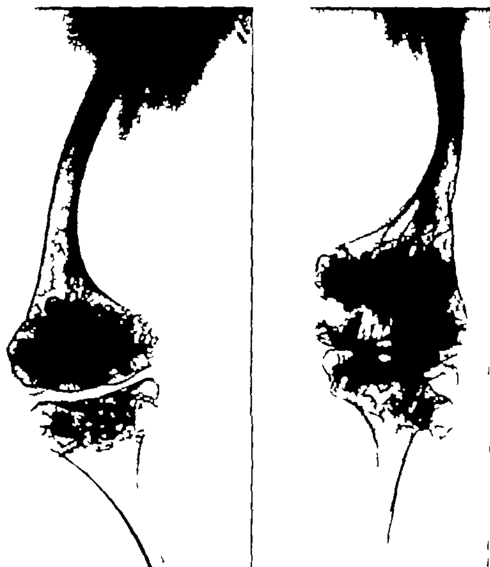


Fig. 23

Case 11—Curious multiple circular opacities or rings in the metaphyses and epiphyses of the femora and tibiae adjacent to the two knee joints Comparable changes were not seen elsewhere in the skeleton.

CASE 12—OSTEOGENESIS IMPERFECTA CYSTICA

(Figs. 24 to 33.) Girl seen at the age of five years and again when eleven years of age

Family history—Father normal. Mother and several members of the mother's family including her father were said to have bluish sclerotics but there was no history of bone fragility. The patient was the third of five children two have blue sclerotics without bone fragility and the others are normal.

Clinical history—History of many fractures the condition was said to be congenital. She was not deaf. The sclerotics were not unusually blue. The head was not of typical shape there was no bulging in the temporal regions. There was scoliosis. Deformity of the pelvis was severe and apparently responsible for faecal obstruction when she was in hospital. She could not walk but made good use of her arms.

Blood examination—Red cells 3·6 million. White cells 8·6 thousand. Lymphocytes 60·5 per cent. Wassermann reaction negative. Slight trace of albumin in urine but blood urea within normal limits. Serum calcium normal (complete investigation of calcium metabolism was impossible). Phosphatase raised (1·42 units—normal 0·1 to 0·2)

Radiographic examination—Honeycombing was distributed throughout the whole skeleton but not in a uniform manner. In the lower limbs it was fairly general but in the upper limbs (at the age of five years) only the metaphyses were cystic. This was strikingly so in the radius and ulna. By the age of eleven years when the condition appeared to have increased in severity this distinction was much less obvious.



FIG. 24

Case 12—Radiograph of tibia when aged 5 years. Note the markedly cystic condition of the whole of the tibia and fibula. The foot shows no special features

Microscopic examination of bone—Microscopic sections of bone from the tibia show medullary spaces filled with loose vascular fibrous tissue.

Subsequent history—By the time the child was eleven years old the deformities had become much more accentuated. At the age of eighteen years the bone changes were universal even the skull showing changes. The girl died when aged twenty-three years.

Fig. 25



Fig. 26

Case 12.—Radiograph of femora and pelvis at the age of 5 years shows almost general cystic condition. There is marked deformity of the pelvis. The inset (Fig. 26) is a microscopic section of a fragment of tibia showing the medullary spaces filled with loose vascular fibrous tissue.



FIG. 27
Case 12—The grossly deformed child when aged 11 years.



FIG. 28
Case 12. Aged 11 years—The whole of the shafts of radius and ulna, and the bones of the hand, are now affected.



FIG. 29

Case 12 Aged 13 years—The upper limbs show generalised cystic changes in all bones, with old and recent fractures.



Fig. 30

Case 12. Aged 18 years—The hand shows almost universal changes.



Fig. 31

Case 1. Aged 18 years—The lower limbs show gross cystic changes, particularly marked at the extremities of the bones.



Fig 32

Case 12. Aged 18 years—Foot showing general changes.



Fig 33

Case 12 Aged 18 years—Skull showing irregular hyperostosis affecting both tables of the skull in the frontal and parietal regions

CASE 13—OSTEOGENESIS IMPERFECTA CYSTICA



Fig. 34

Radiograph of part of a skeleton in the museum of King's College Hospital. The history is unknown. Apparently of adolescent age. Multiple fractures, scoliosis and deformity of the pelvis are seen. The marked cystic structure of the bones seems to justify inclusion in the cystic class of osteogenesis imperfecta.

HYPERPLASTIC CALLUS FORMATION IN OSTEOGENESIS IMPERFECTA

In 1943 Brailsford briefly reported four cases of "a condition suggesting scurvy subperiosteal haemorrhages being more frequent than fractures" occurring as a complication of osteogenesis imperfecta. In 1946 Baker published a paper on "Hyperplastic Callus Simulating Sarcoma in two cases of Fragilitas Ossium" with a detailed study of the histology of the lesions. In 1948 in collaboration with Professor Baker the present author published details of eight cases that developed hyperplastic callus, with a condensed account of the histology. In six of these cases the condition occurred as a complication of osteogenesis imperfecta of the post-natal type. We have since met with one additional case, an elderly woman, almost certainly one of osteogenesis imperfecta. The features in these cases are: a) Formation of unusually dense early local callus not invariably preceded by a recognisable recent fracture. b) Excessive formation of ossified callus, enveloping the shaft of a bone to a varying but quite unusual extent and resulting, in several cases, in permanent enlargement of the bone. Again evidence of a fracture was not always present; occasionally the swelling occurred even without obvious trauma. (c) Formation of bony excrescences on the shafts of long bones with no sign of old fractures.

Both sexes are affected. Excluding the old woman, the age at which the excessive callus was discovered varied from one to fifteen years, but "flares" or new lesions were met with up to twenty four years. What appeared to be an unprovoked "flare" occurred in the old woman after the age of seventy years. In four cases the *early callus* was excessively dense and structureless, in one without obvious signs of a fracture, and this may occur more than once in a bone. The density of the callus suggests excessive calcification while the shape is unusual, the shadow bulging out abruptly from the shaft, like the wings of a butterfly, instead of being fusiform. In each of these cases a femur was affected and in one a humerus in addition. On the femora, but not on the humerus, the dense callus was usually followed by the formation of extensive masses of hyperplastic callus.

The bones affected by *excessive callus formation* were one or both femora in every case, the humerus in four cases, and the radius and ulna less frequently. Excessive callus was not provoked by every fracture in these cases, not even by a second fracture in the same limb. In one case hyperplastic callus and permanent enlargement of one femoral shaft had followed a fracture while a fracture of the other femur healed with only a normal amount of callus. Ten years later this second femur "flared" spontaneously and the whole length of the bone was enveloped in "callus." Radiographs show the callus extends along the shaft far beyond the region which could be affected by the trauma. In these cases, usually but not invariably preceded by a fracture, swelling of the limb occurs to quite an excessive amount with brawny oedema extending even down to the foot when the femur is affected. The superficial veins may be enlarged and even redness of the skin appears. The possibility of sarcoma naturally arises, and biopsy was considered advisable by the surgeon in charge in four of the cases. In one of Brailsford's cases malignant changes actually occurred. With conservative treatment the swelling slowly subsides but frequently some permanent enlargement of the shaft remains.

Bony excrescences were found particularly on the radial and ulnar shafts and also, though with diminishing frequency, on the fibula, tibia, femur, humerus, pelvis, metacarpals and metatarsals. The interosseous borders of the first four bones mentioned were the chief sites.

The cause of the curious features found in these cases is obscure. Brailsford's suggestion of scurvy playing a part is put out of court by the fact that Professor Baker failed to find the faintest sign of haemorrhage, old or recent, in his sections and there was strong evidence against a lack of vitamin C in the cases.

Microscopically the callus in the two cases reported by Baker consisted chiefly of fibromucoid cartilage-like tissue— chondroid tissue. Superficially there was oedema and destruction of muscles, while in the deeper layers the chondroid tissue passed into true cartilage, calcified cartilage and finally woven bone. Knaggs (1926) says that in cases of tabes, fractures may be followed by the formation of a superabundance of callus. Since the cases discussed above are mostly children or adolescents the possibility of tabes playing a part in the clinical picture is excessively remote.

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CASE 14—OSTEOGENESIS IMPERFECTA with HYPERPLASTIC CALLUS

(Figs. 35 to 38.) E. R. female. Normal at birth At seven months swelling of right shoulder followed by swellings of left shoulder and lower ends of both femora. At one year periosteal shadows were present around the shafts of several major long bones. At fourteen months large masses of callus around both femora on the right the callus involved the whole shaft on the left it was of the butterfly type. *The excess of bone about the upper third of the left* humerus was largely absorbed later At nineteen months could crawl but not walk. A month later a fall increased the callus in the left thigh. At nearly three years, lower two-thirds of both femoral shafts were enlarged to about three times the normal. Fall resulted in large bony thickening of lower part of right humerus. Mother stated great swelling invariably occurred if child knocked herself. One attack of nose-bleeding Greenstick fracture of right radius followed by gross thickening Curvature of left femur increased dealt with by osteotomy The periosteum and surface of the bone appeared normal The cortex was eggshell in thickness the medulla soft and fatty " Operation was followed by a flare and great swelling Radiographs of femora at four years were published by Dr Brailsford (1943) At five years, films showed enlargement with cancellous bone of shafts of both femora still present, with many bony excrescences. Mass of intensely dense callus appeared at lower end of left humerus, on inner side preceded by few days pain, but no definite injury and certainly no fracture petechial haemorrhages and hyperaemia appeared in overlying skin, which was tender Child rather small. General osteoporosis of whole skeleton. Radii and ulnae showed several bony excrescences on interosseous borders. Blood normal. Wassermann negative in mother and child. No improvement followed treatment on special vitamin diet. (Under Mr G F Allan.)



FIG. 35

Case 14—Femora, at fourteen months, showing large masses of callus round both shafts. That around the left femur which is almost certainly fractured, is of the butterfly shape and in part denser than normal early callus



FIG. 36

Case 14—Left humerus, at five years, showing dense callus in front of lower end, and sessile bony outgrowth from middle of shaft. No definite injury No fracture.



Fig. 37

Case 14—Femora, at five years, showing gross enlargement of greater part of the shafts, with many bony excrescences.



Fig. 38

Case 14—Left femur two months after osteotomy for anterior bowing, showing intensely dense and apparently structureless, callus on the outer side.

CASE 15—OSTEOGENESIS IMPERFECTA with HYPERPLASTIC CALLUS

(Fig. 39.) P. W. male aged four years followed to thirteen years. History of multiple fractures affecting at least eight bones since age of six months. Rest of family normal. Sclerotics bluish but not typical. Generalised osteoporosis increased with age and prolonged recumbency up to ten years when child first began to walk but only with assistance. Development of early dense callus followed fracture of both femora in the left thigh diffuse hyperplastic callus developed later. Excessive callus also developed around a fractured humerus but this was eventually absorbed. Bony enlargement, of curiously uniform low density of the shaft of the right ulna occurred without a provocative fracture increased over a period of years and finally showed signs of partial absorption. Multiple bony excrescences were a marked feature of the case. Both femoral heads became displaced from the necks. Curious dense mottling developed in the lower femoral and the upper and lower tibial epiphyses. (For the later history and films we are indebted to Mr J. S. Batchelor.)



FIG. 39

Case 15—Right arm showing abnormal formation of new bone, without fracture, along the lateral supracondylar ridge, displacement of the head f the radius, and deformity of the radius and ulna with many bony excrescences along their interosseous borders.

CASE 16—OSTEOGENESIS IMPERFECTA with HYPERPLASTIC CALLUS

(Fig 40) J M. male aged fifteen years. Small thin boy History of at least thirty-eight fractures. Radiographs showed typical fragilitas ossium with innumerable healed fractures. Sustained supracondylar fracture of left femur while getting off bed pan Two weeks later oedema of ankle foot and knee. Abnormally dense callus surrounded the fracture at six weeks. Marked oedema of leg developed with dilated veins over the knee and effusion into the joint Thigh hot swollen and firm. Sarcoma suspected biopsy performed eight weeks after fracture. Section showed hyperplastic callus (Professor Baker) Callus spread till at twenty four weeks, the whole length of the bone was involved. Further fracture occurred in upper third, producing dense nodular callus, and femoral head became displaced from the neck. Swelling gradually subsided but excessive callus was still present from end to end of the bone fifteen months after the injury During this period other fractures occurred in the lower leg no excess of callus developed around these. Three months after the left femur was fractured, the right femur was broken almost spontaneously and a similar mass of excessive callus developed, involving the whole length of the bone. Fracture in the upper limbs resulted in deformity dislocation of both radial heads and limitation of movement of hands. Later another large mass of callus formed spontaneously about the left femur (Under Professor Sir Harry Platt)



Fig. 40

Case 18—Right femur twenty-six weeks after fracture showing an enormous mass of callus filling the thigh and extending up to the neck of the bone The supracondylar fracture is visible The apparent fracture of the callus in the mid-thigh does not involve the femur

CASE 17—OSTEOGENESIS IMPERFECTA (?) with HYPERPLASTIC CALLUS

(Figs. 41 to 43.) A. B., female aged over seventy years. Said to have been bedridden all her life and certainly since the age of four years. Was sure she never went to school. Very backward. Hands clenched and absolutely useless. Incontinent. While in hospital the left arm became swollen spontaneously and the humerus thickened. Sarcoma suspected. Similar "flares" with pain, are said to have affected other bones. Blood examination said to be normal. Unfortunately all her records, except the films, were lost in an air raid. Radiographs show generalised osteoporosis with masses, in some cases enormous of additional bone strongly suggestive of hyperplastic callus around the shafts of many of the long bones. The skull is reduced in vertical measurement and the occipital is protuberant, as seen in some cases of osteogenesis imperfecta. (By courtesy of Dr Grace Batten.)



Fig. 41



Fig. 42



Fig. 43

Fig. 41

Case 17—Right femur showing enormous mass of hyperplastic callus.

Fig. 42

Case 17—Left femur showing mass of callus only slightly smaller than that in right thigh.

Fig. 43

Case 17—Left arm showing the osteoporotic bones and the excess of permanent callus around the lower part of the humerus.

CHAPTER 2

OSTEOPETROSIS

Osteopetrosis generalisata, Marble bones
Albers-Schönberg's disease Osteosclerosis fragilis generalisata

The condition described by Albers-Schönberg in 1904 and to which Karshner (1926) gave the name of osteopetrosis is a rare developmental error the chief characteristic of which is excessive radiographic density of most or all the bones of the skeleton.

Familial and hereditary tendencies—A distinct familial tendency is displayed and the disease is occasionally inherited for example eight cases occurred in three generations (McPeak 1936) It may be transmitted by either sex. Any special features which may be present are constant for a particular family Consanguinity of parents has been noted Nussey (1938) reported consanguinity in twenty three of 112 cases.

Sex—The disease affects both sexes, males slightly more frequently than females.

Age—It has been found at all ages from foetal life to seventy-five years. It undoubtedly begins before birth in some cases and possibly in most

Etiology—The cause is unknown. Rather surprisingly some have believed that parathyroid hyperactivity is responsible (Dupont 1930 Ellis 1934) A tumour of the parathyroid was present in one case but this was regarded, probably correctly as secondary and defensive (Péhu *et al* 1931)

Clinical features—The chief features of the syndrome are abnormal density of the bones with or without fragility a strong tendency to anaemia which may be severe and fatal and optic atrophy The severity and course of the condition vary considerably It may run a benign or a malignant course according to Nussey (1938) benign when the condition is inherited, and malignant when there is consanguinity of the parents. In a well-marked case assuming that the patient survives, the formation of abnormally dense bone continues till growth ceases the condition of the skeleton then remaining stationary at any rate radiographically though it may progress later There may be intermissions, remissions, or complete cessation of the developmental error before growth ceases all of which are demonstrated clearly in X-ray films.

Tendency to fractures—As a rule the bones are intensely hard like marble but bones much softer and more like chalk were present in at least one case (Pirie 1930) A tendency to fracture is certainly present in some cases. One patient sustained ten fractures by the age of twenty years. On the whole fragility of the bones has been much exaggerated. When they occur fractures are sharp abrupt, and transverse Callus formation may be slow

Anaemia—Usually there are no symptoms except those resulting from anaemia, which may become severe enough to call for investigation and may even be fatal at any age It results from reduction of the blood forming marrow in the sclerosed bones and eventually becomes of the aplastic type. Cases in which it was leukaemic and even apparently pernicious in type have been described. The anaemia is a source of real danger but it by no means corresponds always to the severity of the bone condition. A woman lived to the age of seventy five years in spite of advanced petrosis of the whole skeleton and yet section of a femur in this case showed complete obliteration of the medullary cavity Apart from the anaemia blood examination reveals nothing of importance The serum calcium is usually normal but it is raised occasionally When generalised calcinosis is present the serum calcium may even be doubled (Schulze 1941) The plasma phosphatase is either normal or slightly low Children displaying

widespread abnormal deposits of calcium salts in the body may or may not have osteopetrosis in addition. If anaemia is severe compensatory enlargement of the spleen, liver and lymph glands may be present.

Optic atrophy—Optic atrophy may result from changes in the base of the skull but it is frequently absent. It has been seen as early as the sixth month of life. Nystagmus, hydrocephalus facial or ocular palsy and deafness are other not very uncommon complications. The teeth are prone to decay Some degree of dwarfism is often present. Osteomyelitis is stated to be not uncommon.

Radiographic features—As seen in radiographs the extent to which bones are affected varies considerably The whole of a bone including the epiphyses may be uniformly dense and completely structureless. With rays of sufficient hardness fine striations both transverse and longitudinal may be made out in the metaphyses and epiphyses (Sear 1927) Occasionally less dense areas may be seen in the sclerosed bone. The parts unaffected by petrosis may show osteoporosis but this is sometimes more apparent than real. As a rule metaphyses are more affected than shafts of the long bones they are commonly enlarged or clubbed, the enlargement ending abruptly at its junction with the diaphysis Occasionally the reverse holds good the diaphyses being more affected with the metaphyses less dense and either normal in shape or clubbed (Ellis 1934) A streaky or patchy arrangement of the denser bone is very rarely seen in cases of generalised osteopetrosis. Apart from clubbing, the shape of bones in both varieties is unaffected. In some cases a narrow clear transverse band marks the junction of diaphysis and enlarged metaphysis in others, dense and less dense bands alternate The unusual distribution of dense bone may suggest the markings of a zebra. The clavicles the lower part of the humerus and the radius and the ulna may show less density than the rest of the skeleton. If in a child, the tendency to form petrosed bone ceases suddenly after a time the epiphyses will show a dense centre surrounded by a halo of bone of normal density The ilia often show alternating dense and clear curved bands parallel to the cresta. The carpal and tarsal bones, though sometimes universally dense or mottled, frequently show a dense centre surrounded by a halo of clearer bone or the reverse may be seen when the pathological change began later than usual. Alternating concentric rings of dense and clear bone are not uncommon. As a rule the phalanges are decidedly less affected than the rest of the skeleton and they show a dense transverse band of varying width in the metaphysis, close to or a short distance from, the epiphyseal lines. In milder cases these bands are a striking feature of the hands. Similar dark bands in the phalanges and at the ends of the long bones may however result from the absorption and deposition of lead, phosphorus, or bismuth. *The skull* shows the expected degree of density which is particularly marked at the base. The pituitary fossa is usually rather small and the posterior clinoid processes are thick and clubbed, almost closing in the fossa. The air sinuses are invisible the frontal and nasal bones may be thickened as well as dense The maxillae may be affected but the mandible almost invariably escapes. Calcification of the dural folds may be seen. The vertebral bodies if not uniformly dense usually present two horizontal bands of dense bone above and below with a less dense band between. The ribs are affected, sometimes irregularly but the rib cartilages escape In cases complicated by a tendency to generalised calcinosis, calcification may be seen even in children in the main arteries of the limbs, in the ligaments *the larger tendons the kidneys the walls of the trachea*, the stomach and in other soft tissues. Coxa vara, not the result of fracture may be present it was seen in three brothers all of whom showed generalised osteopetrosis. The deformity may be of the infantile or cervical type.

Pathological features—The petrosed bone is white-grey on section. The shaft of a long bone may be completely solid with the medullary cavity obliterated. The pathological changes are essentially sclerotic in nature with increase in number and thickness of trabeculae The architecture is disorderly and irregular There may also be hypercalcification of

cartilage with persistence of nodules of calcified cartilage in the zone of newly formed trabeculae. (McCune and Bradley 1934) The density may be increased further by deposition of calcium salts in the reduced medullary spaces when general calcinosis is also present. Spherical foci of ossification appear in the calcified cartilage. No fatty marrow is to be seen what marrow there is being myeloid. Osteoblasts are either normal or increased in number osteoclasts may be normal in number or absent. An important change found in the marrow is fibrosis. It has been suggested—and this seems quite possible—that in some cases the severity of the anaemia depends more on fibrosis of the marrow than on reduction of the marrow space by sclerosis. Reports on the chemistry are confusing but it seems clear that the ossified bone matrix is normal in composition.

Diagnosis—The diagnosis is usually easy when radiographic examination has once been decided upon. In mild cases chronic poisoning with lead or phosphorus must be excluded while in certain localities even in this country fluorosis is worthy of consideration. Jupe (1938) reported in two cretins the finding of juxta-epiphysial dense bands in the metaphyses which disappeared under treatment. Occasionally limited distribution of the dense bone may give rise to difficulty in classification such cases are probably best placed in the melorheostosis group.

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CASE 18—OSTEOPETROSIS—Severe Type

(Figs. 44 to 49) E. L. girl aged 7 years. Genu valgum Flat feet Bilateral optic atrophy left eye practically blind Toes and fingers clubbed and oedematous. *Blood*—Red cells 3 912,000 White cells 5000 Haemoglobin 47 per cent Colour index, 53 Right femur fractured by fall and left femur fractured during application of tourniquet. (Under Mr McCrae Aitken.)



FIG 44

Case 18—The shoulder upper ribs and spine show uniform increment of all bones in the film. In the humerus there is ... of the epiphyses the metaphysis and shaft are enlarged (clubbed) and dense



Fig. 45



Fig. 46



Fig. 47

Case 18—The foot (Fig. 45) shows every bone affected, the intensity being most marked in the tarsus, decreasing progressively towards the tips of the toes. Note that the metatarsals show general increased density which is greatest in the metaphyses, whereas in the phalanges the petrosis is almost confined to the metaphyseal regions where the dense bone shows transverse striation. The hand (Fig. 46) shows distribution of petrosis similar to that of the foot. The carpal bones show uniform density. In the region of the knee joint (Fig. 47) there is very abrupt change from the less dense shafts of the femur and tibia to the more dense metaphyses. Note the obvious "clubbing" of these extremities with suggestion of cross striation in the tibia and fibula and some longitudinal striation in the femur. The epiphyses are as dense as the metaphyses.



FIG. 48



FIG. 49

CASE 18.—The skull (Fig. 48) is somewhat thickened and shows abnormal density especially of the base. There is no sign of the frontal sinuses. The pituitary fossa is rather small and the posterior clinoid processes are clubbed. There is some increased density of the maxillae but not of the mandible. The pelvis and upper femora (Fig. 49) show marked "clubbing" of the femur on each side and complete lack of structure except the epiphysial lines. The sacrum is less affected. In the iliac bones, alternate dense and less dense bands are well seen. There is a curious vertical band of less dense bone in the upper part of the necks of both femora.

CASE 19—OSTEOPETROSIS

(Figs 50 to 53.) Half-caste Australian girl, aged two and a half years who had never walked or talked. The parents and one sister were said to be normal. There was a slight squint and advanced optic atrophy Anaemia and splenomegaly had been present for nearly two years. There was hypotonia of muscles and muscular wasting The bones were easily palpable and the ends of the long bones were felt to be much enlarged. *Blood examination*—Red cells, 3 000 000 White cells 10 000 Haemoglobin 21 per cent. Wassermann negative. Blood calcium and phosphorus normal. (Under Dr Verco of Adelaide.)



FIG 50

Case 19—The tibiae and fibulae show well marked clubbing and clear bands with some longitudinal striation toward both extremities of the bones The bones of the feet were not well seen but were obviously dense The upper tibial epiphyses show a less zone surrounded by denser bone and enclosing a dense central area



Fig. 51



Fig. 52



Fig. 53

Case 19—The skull (Fig. 51) shows increased density especially of the base and a small pituitary fossa with enlarged posterior clinoids. The lower jaw is strikingly normal in density but the maxillæ are petrosed. The lower limbs (Fig. 52) show increased density and loss of the normal architecture of all bones. Clubbing of the metaphyses is striking, being most marked at the lower ends of the femora. Clear bands are seen corresponding roughly with the junction of shafts and metaphyses. The upper tibial epiphysis shows a clear ring encircling and surrounded by denser bone. Clear bands are also seen in the lower thirds of the forearm bones and metacarpals (Fig. 53) accompanied by slight enlargement. There is a healed fracture of the left ulna. The phalanges, as usual, are less affected than the rest of the skeleton, and they display no clubbing.

CASE 20—OSTEOPETROSIS—Benign Type

(Figs. 54 to 58.) H. R. girl aged six years. Condition inherited from the mother who is mildly affected (Case 21. Fig. 59). There was no history of fractures. The child was admitted to hospital for septic arthritis of the left hip joint. Radiographic investigation showed clear evidence of a benign degree of osteopetrosis. *Blood examination*—Red cells 4 600 000. White cells 11 800. Haemoglobin, 75 per cent. Red cells normal. Serum calcium rather high (12·8 mg.). phosphorus normal (5·6 mg.). No sign of optic neuritis. (Under the late Sir Henry Gauvain.)



Fig. 54

Case 20—Pelvis and upper femora showing an unusual number of narrow alternating bands parallel to the iliac crests. The femora are both affected in a somewhat patchy and unusual way, the appearance of the upper femoral shafts being rather suggestive of that seen in some cases of diffuse fibrosis of bone. The changes in the region of the left hip joint are due to the infection of the hip joint with resulting decalcification causing less density of the left side of the pelvis and left femur than on the right side.



Fig 55



Fig. 56



Fig. 57

Case 70—The knee joints (Fig 55) show alternate dark and light transverse bands with greatest density at the ends of the metaphyses suggesting that the tendency to formation of osteopetrotic bone is becoming more marked The bands are broader and less sharply defined than the so-called lines of arrested growth. Dense bone in the epiphyses is distributed irregularly The foot (Fig 56) shows unusual patchy distribution of dense bone in the metatarsals typical bands in the phalanges which are parallel with but not adjacent to the epiphyseal lines and well-marked single or double rings in the tarsal bones In the hand (Fig 57) there are dense bands and irregular areas of density in most bones Note that the cortical bone seems less affected than the endosteal bone All four inner metacarpals show a dense band at their bases while only two show density towards the distal or growing end Dense bands in the phalanges are some distance from the epiphyseal lines and not in the most recently formed bone as in Fig 55 The larger carpal bones show single dark circles



FIG. 58

Case 20—The spine shows clearly the three bands in the vertebral bodies—a lighter band between two dark bands. The ribs show some increased density but they are not strikingly affected.

CASE 21—OSTEOPETROSIS—Mildest Type

(Fig 59) Mrs R. mother of patient Case 20. In perfect health. Dense bone was seen only at or near the ends of long bones. The outer condyle of the one femur that was X-rayed and the outer tuberosity of the corresponding tibia were more dense than the inner



Fig 59

Case 21—Hand showing similar distribution of dense bone to that seen in her daughter (Fig 57) The somewhat erratic distribution in the distal parts of the two innermost metacarpals is strikingly similar in the two cases.

CASE 22—OSTEOPETROSIS

(Figs. 60 to 65.) K. L. woman aged seventy three years. The bone condition was discovered by accident after admission for a fracture of the femur. Spleen not enlarged. No anaemia. No optic atrophy. Blood examination negative. Right femur had been fractured twice and left femur once. Died at age seventy five years. (Under Dr W. J. Gill.)



Fig. 60

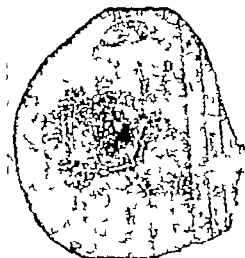


Fig. 61

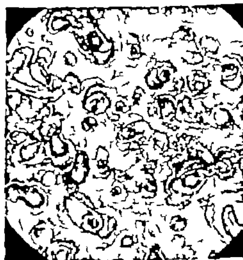


Fig. 62

Case 22—The hands (Fig. 60) show well-marked petrosis of all long bones. Note the alternating bands in the proximal phalanges. The lower epiphyses of radius and ulna and the carpal bones are partly involved. Cross section of the shaft of the femur (Fig. 61) shows complete obliteration of the medullary cavity (the dark patch is an artefact). Microscopic section of the femur (Fig. 62) shows the curious architecture of the dense bone. (By courtesy of Professor W. G. Barnard.)



Fig. 63



Fig. 64



Fig. 65

Case ??.—The pelvis (Fig. 63) shows generally increased density to a marked degree; there are no definite curved bands in the ilia. Old fracture neck of right femur. The skull (Fig. 64) shows increased density particularly at the base. The pituitary fossa is slightly small. The frontal sinuses are not visible. The density of the facial bones and lower jaw is apparently normal. The cervical vertebrae are dense. The lower limb (Fig. 65) shows almost complete obliteration of structure of all bones including the patella. There is arthritic lipping of the knee joint.

CASE 23—OSTEOPETROSIS

(Figs. 66 to 70.) C. R. boy aged nineteen months. Admitted to hospital because of general backwardness and failure to gain weight. Right facial palsy. No history of fractures. *Blood examination*—serum calcium 13·5 mg. per cent. Blood cholesterol 162 mg. Haemoglobin, 84 per cent. Wassermann and Kahn reactions negative. (Under Professor Alan Moncrieff.)

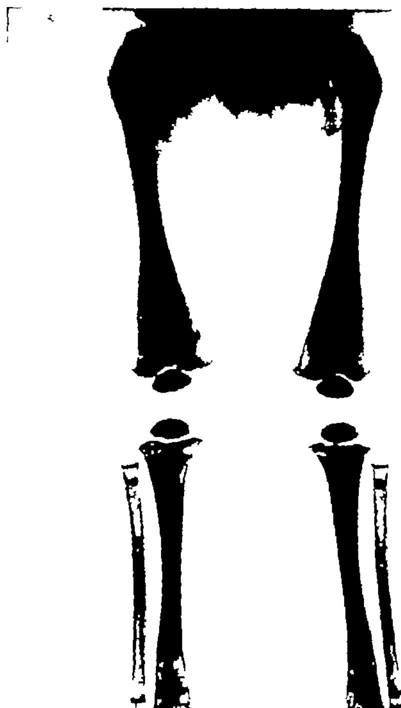


FIG. 66

CASE 23.—November 1945. The lower limbs show general increased density of long bones ending abruptly above and below in intensely opaque bands a short distance from the epiphyseal lines. Recently formed bone in the metaphyses is distinctly less dense than in the rest of the shafts.

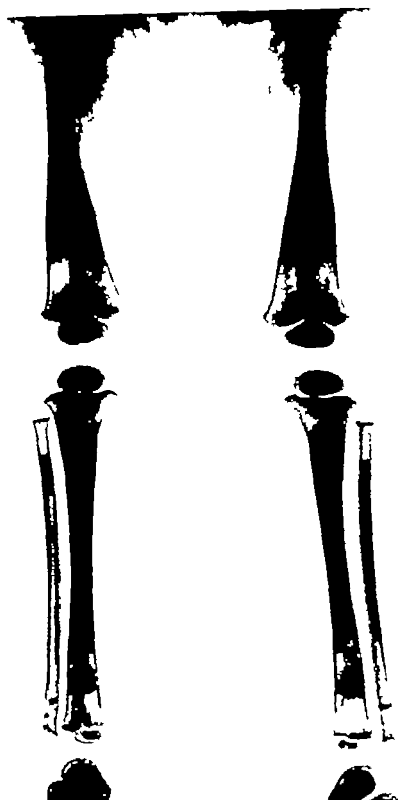


Fig. 67

Case 3— July 1948. Film taken for comparison with Fig. 66. Note that bone added during the interval of eight months has been unaffected by petrosis—in fact it is somewhat porotic. New bone formed around the abnormally dense epiphyseal nuclei is of normal density. The same is true of the tarsal bones.



FIG. 68

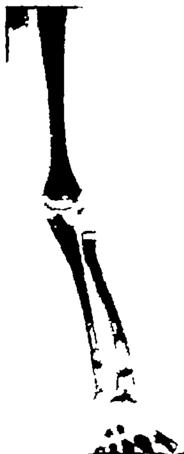


FIG. 69



FIG. 70

CASE 23—July 1946 Radiographs of the upper limbs (Fig 69) show similar distribution and extent of density as in the lower limbs The skull (Fig 68) shows increased density notably of the base with thickening in the frontal region. The pituitary fossa is small. The maxilla are affected. There is increased density of vertebrae sacrum ribs and sternum (Fig 70)

CASE 24—OSTEOPETROSIS

(Figs. 71 to 74) R. P boy aged five years. Admitted to hospital for pain in the region of the left hip joint of some months duration. No optic neuritis. *Blood examination*—Red cells 4,300 000 Haemoglobin 90 per cent White cells 2 600 (Nine days later 6000) Neutrophils 40 per cent. Lymphocytes 56 per cent Chemical analysis showed no abnormality The evidence suggested an atypical case of osteopetrosis. (Under Mr D B Craig)



FIG. 71



FIG. 72

Case 24—The shafts of the femora (Fig 71) show unusual distribution of increased density particularly in the region of the knee joints. There is marked longitudinal striation of the metaphyses. Not what appears to be a chip fracture of the neck of the left femur with minimal displacement of the head, suggestive of the infantile type of coxa vara The spine (Fig 72) shows abnormal density of the upper and lower parts of each body with a less dense band between, which is strong evidence in favour of the diagnosis of osteopetrosis



Fig 73



Fig 74

Case 24—The skull (Fig 73) shows abnormal density particularly of the base The pituitary fossa is small The upper and possibly the lower jaw seem to be affected The pelvis and hips (Fig 74) show fairly generalised osteopetrosis There are faint bands parallel with the crests The fracture of the neck of the femur suggestive of infantile cases are again shown in this film

CHAPTER 3

MELORHEOSTOSIS

Synonyms—Léri type of osteopetrosis
Osteosi eburnizzante monomelica (Putti)

Melorheostosis is a very rare condition in which certain bones, or parts of bones are petrosed. It displays striking differences from generalised osteopetrosis or marble bones. Briefly the distinguishing features are 1) the changes in typical cases are confined to the bones of one limb 2) the outline of an affected bone is sooner or later distorted 3) there is often pain occasionally severe sometimes unbearable 4) there is limitation of movement in the joints formed by the affected bones. None of these features is invariably present and each demands further consideration

Léri and Joanny (1922) published the first case in which an arm was affected and suggested the descriptive title melorheostosis which is now widely adopted, the distribution of dense areas suggesting to them the flow of candle-grease down the limb. In 1927 Putti described two cases both with a lower limb affected under the other descriptive title osteosi eburnizzante monomelica. More than forty other cases have been reported under various titles some of which I regard as erroneous. In this country only four unquestionable cases of melorheostosis have been reported (Wakeley 1931 Boggon 1938 Franklin and Matheson 1942 Le Vay 1946)

Hereditary and familial influences play no part in this affection.

Sex—The condition may be observed in both sexes males being affected rather more commonly than females.

Age—In reported cases the ages varied from five to fifty four years. If one case is included in which half the pelvis and the whole of the corresponding femur were affected the upper age limit is seventy-one years (Rendu and Gay 1929) Three-quarters of the forty seven cases studied were under thirty-six years of age. It probably begins in childhood in all cases. There is however strong presumptive evidence that at least occasionally it begins in foetal life. In three cases deformity of a digit was noticed at birth and this was later shown to be the result of typical hyperostotic changes in certain bones of the hand (Junghagen 1930 Léri, Loiseleur and Lièvre 1930 Widman and Stecher 1935)

Etiology—The cause is entirely unknown. Ischaemia secondary to local disturbance of the sympathetic system was suggested by Putti, but the theory which rightly has received greatest support is that it is a developmental error the result of embryonic metameric disturbance (Zimmer 1937)

Distribution of the petrosis—The arm is affected less often than the leg which was involved in three-fifths of thirty nine monomelic cases. The two lower limbs are equally susceptible but the right arm is more often affected than the left. Typically the changes are confined to one limb but search of the literature has revealed seven cases in which more than one limb was the seat of changes strongly suggestive of melorheostosis (though at the time of publication this was regarded as the diagnosis in only four) One of these is certainly atypical and must be regarded as questionable (Hall 1940) The records of an eighth case as yet unpublished with both legs and one arm affected have been examined by courtesy of Dr W Mackenzie. In the seven reported cases both legs were affected in four both arms in one the right arm and leg in one and all four limbs in one. In the last case it is difficult to avoid the conclusion that changes typical of both melorheostosis and osteopoikilosis were present though it was reported only under the title of osteopoikilosis (Nichols and Shiflett 1934)

Symptoms and signs—Pain is the most frequent symptom. It is complained of at some time in half the cases. The older the patient the more likely is pain to be a feature. The earliest age at which pain was reported was eight years (Putti 1927) The pain is usually dull and aching in character sometimes it is felt only on exertion seldom is it severe
Limitation of movement of one or more joints of the affected limb is found in nearly half the cases and is more likely to occur late than early It is due to the excessive formation of dense bone in the immediate neighbourhood of a joint and to the deposition of bone in soft tissues rather than to actual distortion of the articular surfaces There may be swelling of the limb oedema, and induration. Erythema of skin over the affected parts of a hand has been reported. Nodular induration of the tissues may be present and occasionally irregular thickening of a bone may be felt easily particularly when the phalanges are affected. Progressive wasting of the limb may occur Diminished sensibility and tingling have been noted but only in two or three cases In one there was tenderness of the tibia (Nichols and Shiflett 1934)
Shortening of the limb has been a feature in some cases (two upper nine lower limbs) while less frequently the affected limb has been *longer* than its fellow (one upper three lower limbs) *Deformities* due to bone thickening coupled with limited movement of one or more digits of the hand *are not uncommon when the upper limb is involved (seven of sixteen upper limb* cases) Pes valgus genu valgum curvature of a bone and enlargement of a knee have all been reported as being responsible for discovery of the condition of the bone.

Other initial signs and symptoms which called attention to the affected limb were pain scleroderma, and stiffness. Though in most cases the first complaint is made before growth has ceased the onset of symptoms may be delayed considerably in spite of advanced changes in the affected bones. There is no undue fragility of the petrosed bones.

Complications—*Scleroderma* with fibrosis and thickening of muscles and other soft tissues, *may be responsible occasionally for stiffness. These fibrotic complications which may precede* the bone changes have sometimes been reported in association with melorheostosis the soft tissue changes corresponding more or less to the distribution of the bone changes (Gillespie and Siegling 1938 Dillehunt and Chuinard 1936 Clémont and Combes-Hamelle 194*)
Blood examination reveals nothing of importance. High phosphatase as in Franklin and Matheson s case is of no significance

Radiographic appearances—In well marked cases radiographs show that some parts, *and less commonly the whole of certain bones throughout the length of the limb* have the dense structureless appearance of marble bones. At first glance the flow of dense streaks and blotches—a flow which may be limited to part of a limb and may be interrupted or continuous—seems to follow the distribution of a main vessel or nerve even to the finger tips but this does not bear more close investigation It is common to see one side of a long bone escape either for part or all of its length, while the other side is dense and thickened. In the forearm and leg respectively it is quite typical to find that one bone is affected while the other is normal Only very seldom is the flow limited to a single bone The scapula or the half pelvis corresponding to the affected limb usually shows dense patches and spots. Sclerosed bone may be endosteal or cortical but it is usually present in both situations in a long bone The later a case is examined the more likely is it that there will be cortical distortion With few exceptions dense patches in the carpus and tarsus are entirely endosteal. Cortical thickening and distortion of outline of the affected bones seem to be more common features in the arm than in the leg In some cases density in a long bone ends above or below in streaks not unlike those seen in diffuse fibrosis of bone and these streaks may extend into the adjacent epiphysis In the epiphyses and short bones the dense areas usually take the form of splashes streaks or dots It is quite common however and by some it is regarded

as typical for the region of a joint to be skipped the earlier the case the more likely is this to be so As already stated the bones are sometimes affected close up to a joint the movement of which may be restricted.

Curvature either apparent or real may be present when one side of a bone is markedly distorted by extensive petrosis. Deposits of bone in soft tissues have been seen in the regions of the hip knee shoulder ankle and foot Decalcification of bone in the nieghbourhood of dense areas has been noted, and occasionally cyst-like cavities have been seen near or even in a dense patch sometimes these changes are more apparent than real. Though the density varies in intensity in different cases or in different bones of a case it is usually uniform and smooth.

The skull spine and ribs almost invariably escape but all were affected in Franklin and Matheson s unquestionable case in which the right arm and leg were both the seat of typical changes and which was remarkable in that the right half of the mandible was grossly thickened and very dense. No other case with involvement of the jaw has been reported. The skull was also affected in two patients reported by Hall (1940) one an atypical case affecting both upper limbs and the other a case which must I think, be regarded as questionable The fourth rib was dense in an arm case of limited distribution (Weil and Weissman-Netter 1932) the sixth rib was involved in Dr Mackenzie s case. The *sacrum* was affected on one side in a case in which both legs showed extensive changes (Baker and Jones 1941) and in the later films of Wakeley's case in which both legs were also affected. The *patella* was affected in at least five cases, and the *clavicle* only in one.

Progress—Probably in most cases the bone changes are progressive in some this has been proved as for example in Léri and Joanny s original case which was observed over a period of seven years. Wakeley s case reported as one of marble bones but which I think should be classified as melorheostosis was re-examined after thirteen years and extension of the lesions had unquestionably occurred. On the other hand the lesions are not invariably progressive a boy aged five years with a leg affected was re-examined at the age of twelve years and no change was reported (Kibby 1941) Extension of lesions already present seems to be more common than the appearance of fresh areas of density although the latter may certainly occur

Pathology—Histological reports available in nine cases, some of which are conflicting and not very helpful indicate that dense areas are the seat of sclerosis with compact over crowding of lamellae arranged in a bizarre manner there is an interlacing pattern of immature and adult bone Concentric perivascular ossification is sometimes mentioned and in two cases—but only in two—there was definite fibrosis of the marrow

Diagnosis in a typical case is easy In generalised osteopetrosis every bone is affected to some extent and the distribution of the density in individual bones differs markedly from that seen in melorheostosis. From osteopoikilosis the differentiation is also easy provided that the whole radiographic evidence is considered and that undue attention is not paid to the appearance of one or two epiphyses. Osteopoikilosis is a general affection of the skeleton and it is not confined to one limb as melorheostosis usually is moreover it is never associated with opacities in the soft tissues.

Multiple diffuse fibrosis of bone (polyostotic fibrous dysplasia) and Albright s syndrome may give in an individual bone an appearance suggestive of melorheostosis the fibrotic portion of the bone being unusually dense not cystic and having an abrupt outline But in multiple diffuse fibrosis and Albright s syndrome the epiphyses carpus and tarsus are not affected and the dense areas are not so dense and lacking in structure as in melorheostosis. In cases of fibrosis one or more metacarpals or metatarsals are not uncommonly involved, but they show general enlargement of the shafts which tend to be of uniform density with

minimal indication of a cortex while in melorheostosis the change is that of an asymmetrical or local enlargement, with distortion of the surface by intensely sclerotic bone

No difficulty should be experienced in distinguishing the osteopetrosis of melorheostosis from inflammatory sclerosis.

Difference of opinion as to the classification of individual cases is bound to occur sometimes as it has done not infrequently in the past.

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CASE 25—MELORHEOSTOSIS OF ONE ARM

(Fig 73) Woman aged thirty nine years. Complained of pain in the left arm for three years. Deformity of the middle finger present for nearly thirty years. Limitation of movement to varying degree of all joints of the limb Patient kept under observation for seven years changes found to be progressive (Case published by Léri and Joanny 1922 and Léri and Lièvre 1928)



Case 25—Diagrammatic reconstruction of published films to show distribution of the petrosed bone Note the involvement of part of several bones and the distortion of their surfaces The flection of both bones of the forearm is unusual

FIG. 73

CASE 26—MELORHEOSTOSIS OF ONE ARM

(Figs. 76 and 77) Adult male. Always had swelling on the dorsum of the right hand. Complained of stiffness of the middle finger. Some limitation of movement of the elbow, wrist and affected fingers. Palpable nodules on the phalanges. (Case published by Junghagen 1930.)

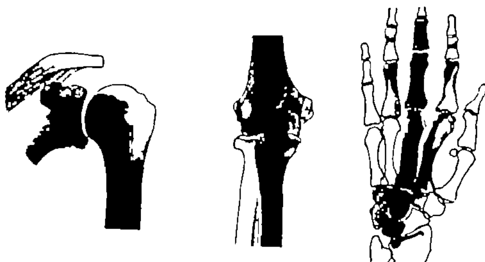


Fig. 76

Case 26—Drawings of the published films showing distribution of the "flow." Note the curious shape of dense bone in the lower end of the radius and the single dot similar to those seen in osteopoikilosis in the lower end of the ulna.



Fig. 77

Case 26—Microscopic section of fragment of the olecranon showing pattern of the sclerosed bone.

CASE 27—MELORHEOSTOSIS AFFECTING ONE LOWER LIMB

(Figs. 78 to 82.) Male aged thirty years. Complained of ulcers of the right leg and of pain in the right ankle. When aged twelve years sustained a fracture of the right foot. Served in the Police Force for the past ten years. Eighteen months ago noticed swelling on outer side of the right ankle with aching pain in the joint. Swelling increased for a year and then remained stationary. Has had more pain recently. Ulcers on the right leg formed a few weeks before examination. Several painless subcutaneous nodules felt in the right leg and thigh. Radiographs show typical melorheostosis of the right leg, affecting to a varying extent the pelvis, outer femoral condyle, fibula, astragalus, os calcis, cuboid, outer cuneiform, three outer metatarsals and corresponding phalanges. Wassermann and Kahn reactions both positive. After antisyphilitic treatment the gummatous ulcers healed rapidly, but there was no change in the bone condition. (Report of the case by Boggon in 1938 included no radiographs.)

Eight years later the patient reported that the right ankle ached occasionally in wet weather and after a heavy day's work. He was still in the police force. Radiographs showed slight increase of dense bone over the outer side of fibula above the lateral malleolus, in one metatarsal and in the os calcis and cuboid. The calcaneo-cuboid joint was completely obscured. A small opacity, seen in an earlier film in the soft tissues near the lesser trochanter, had increased in size. Several other opacities, irregular in shape and fragmented, had appeared in the popliteal region. The opacities behind the ankle joint, visible when he was first examined, had become more consolidated. (By courtesy of Mr R. H. Boggon and the kind help of Dr W. Arklay Steel.)



Fig. 78

Case 27—Pelvis (1939) showing dense bone in and on the surface of the right ischium and pubis.



Fig 79

Case 27—Right knee (1947) showing dense bone in the lower end of the femur one spot in the tibia and a dense area in the fibula which extends into the head f the bone. Not opacities in th soft tissues behind the joint.



Fig. 80



Fig. 81a



Fig. 81b

Case 27—Fig 80 (print reversed) show the right foot 1938 There wer irregular dense areas n the stragalus s calcis cuboid outer metatarsal and phalanges Not the dist rtion f outline of the cuboid nd fifth metatarsal and the multipl opacities n soft tissues behind th tragalus Fig 81 show the same foot in 1947 there is extension of dense bone f rmation the alcaneo-c boid jo nt no longer isibl Not onsolidat on of opacities behind ankle Antero-posterior iew show distribution of petrosed bone in metatarsals and phalanges

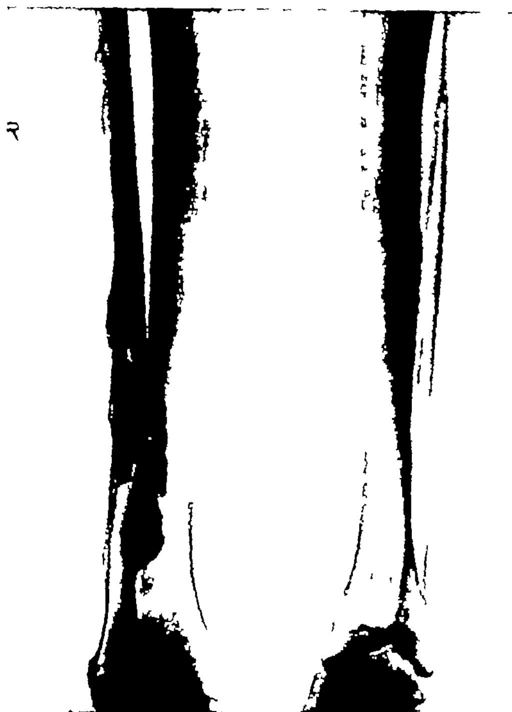


Fig 61

Case 27—(1938) Right and left legs, showing marked changes in the right fibula with much subperiosteal hyperostosis The right tibia is normal except for a small area in the lower third

CASE 28—MELORHEOSTOSIS—Unusual case affecting both lower limbs

(Figs. 83 to 87.) Male aged twenty years. No symptoms referable to the abnormal bones. Condition discovered at the age of eight years when he was examined for limp due to flat foot. No other case in the family. Reported by Wakely (1931) as a case of marble bones and by the author (1930) as one of melorheostosis. Served in the Royal Air Force. Admitted to hospital for injury, re-examined and further radiographs taken in 1944. Lesions in the bones of both legs have definitely progressed. The change of diagnosis to melorheostosis seems to be justified. (By courtesy of Sir Reginald Watson-Jones.)



FIG. 83

Case 28—Pelvis and upper femora in 1944. Note involvement of the femoral heads which were unaffected in 1931. Both femoral shafts now show thickening on the outer sides. Dense area in the pelvis has extended and they now involve the sacrum on the right side. Note the decalcified areas in the pelvis and in the greater trochanters.

CHAPTER 4

DIAPHYSIAL ACLASIS

Synonyms—Multiple exostoses, Hereditary deforming chondrodysplasia

The condition to which the name of diaphysial aclasis was given by Keith (1910) at the suggestion of a friend is characterised by the presence of cancellous exostoses capped with cartilage and by failure on the part of the periosteum to model the metaphyses of long bones in a normal manner. Diaphysial aclasis and dyschondroplasia are often regarded as variations of one and the same developmental error and they are frequently confused, but with little if any justification. Both result from a fault of the epiphysial plate—nests of *cartilage becoming misplaced, instead of being calcified and ossified in the normal manner*—but radiographically they are quite different and in the vast majority of cases they are distinguishable without the slightest difficulty. Exostoses are outgrowths of cancellous *bone on the surface of the parent bone; dyschondroplasia, on the other hand, is characterised* by columns or masses of cartilage lying inside the metaphyses, that is to say the lesions are essentially endosteal.

Hereditary and familial influences play a definite part in the incidence. Stocks and Barrington (1925) found evidence of hereditary factors in 65 per cent. of 1 105 cases. It may be transmitted by both males and females and is said to affect about half the offspring of a *person showing evidence of the condition. It has been traced through as many as five* generations (Reinecke 1891).

Sex—Of the reported cases two-thirds are males. *Age*—Though sometimes present at birth it seldom causes trouble before the age of six years and perhaps not till after growth has ceased. *Etiology*—The cause is entirely unknown.

Incidence.—The number of exostoses in a single patient may vary from one to a thousand (*Stocks and Barrington 1925*); one or two dozen are quite common. *The size also varies* considerably. A single exostosis may grow to a size sufficient to give rise to symptoms and so may two or three exostoses in a multiple case although most of them remain too small to *be of clinical importance. The bones affected chiefly, but not exclusively, as suggested by* Keith, are the long bones which are formed in cartilage with help from the periosteum. The exostoses project from the surface of the metaphyses or adjacent parts of the shafts and are *particularly common near the ends at which growth is greatest.* The more recent the outgrowth the nearer it lies to the epiphysial line—the distance naturally increasing as the bone grows. Exostoses attached to the middle third of the shaft of a long bone—a site indicating very early origin—are rare. The epiphyses are never the seat of exostoses. The most common sites are the femur and tibia in the region of the knee joint, the upper end of the humerus, both ends of the fibula, and the lower ends of the radius and ulna. The pelvis (most commonly the ilia), the clavicles, sternum, spine, mandible, ribs (anterior ends), carpus, tarsus, and scapulae show outgrowths less frequently. Exostoses are seldom seen in the neighbourhood of the elbow joint. In the spine it is the neural arches that are affected and only very seldom a vertebral body; spinal exostoses are usually small. The author has seen only two cases with large exostoses of the spine. The metacarpals and phalanges may show small projections from the cortex, usually close to the epiphysial lines, though occasionally nearer the centre of the shaft, but the changes are insignificant and they are in sharp contrast to the crippling deformities of the fingers which are often produced by the enchondromata of dyschondroplasia. In a few cases exostoses have been described on the sternum and in the sub-occipital and mastoid regions of the skull; they may even occur on the vertex of the skull.

when they are said to be similar to isolated cranial osteomata (Stocks and Barrington 1925)
Dwarfing—There is often but by no means always a varying degree of general dwarfing There may be inequality in the length of the limbs, though it is not always the more affected which is the shorter

Symptoms and signs—Most of the exostoses cause no symptoms but a few from their size and position give rise to some discomfort in surrounding structures For instance an exostosis on the inner side of the femur or tibia may cause inconvenience by pressure against the other leg or against a saddle during riding A muscle or tendon may slip to and fro over the bony projection and produce an inflammatory reaction in the bursa covering the cartilage cap Occasionally abrupt slipping of a tendon produces a snap and this may even cause temporary locking of the adjacent joint Advice may be sought by reason of pain impaired function, size of the growth or deformity and in quite exceptional cases interference with a nerve or artery Very occasionally paraplegia has resulted from the pressure of a vertebral exostosis usually one situated in the cervical region. In common with certain other conditions the ulna is often unduly short with its lower end imperfectly developed and with an exostosis projecting from the lower third of one or both forearm bones. The shaft of the radius is curved and the head of the bone is not infrequently dislocated. Even when there is no such dislocation, the relative position of the humeral condyles may be abnormal. The lower articular surface of the radius is tilted inwards and there is displacement inwards of the carpus but usually without ulnar deviation of the hand. Deformity of the forearm may be unilateral or bilateral. The fibula may be short, but much less frequently than the ulna. Shortening of the fibula, unaccompanied by deformity of the tibia, is more often obvious at the upper end than at the lower The lower ends of the tibia and fibula, distorted by bony outgrowths are sometimes said to be fused but if true fusion occurs at all it is very rare

Radiographic appearances—Radiographs show that individual exostoses have broad bases fused with the shaft of the parent bone. Some are sessile projections but when the exostosis is well formed the shape is always characteristic on the side nearer the centre of the shaft the projection of bone rises abruptly almost at right angles to the surface of the shaft whereas on the other side it slopes gradually towards the epiphysis The apex is directed towards the centre of the bone and though occasionally ending in a sharp point it is more often rounded, with a tendency to become enlarged or mushroomed. Sometimes the enlargement is irregular and resembles a cauliflower An important additional feature often absent when there are no more than one or two exostoses but always seen when these are numerous is irregular enlargement and abnormal shape of the metaphyses and adjacent parts of the shafts. The periosteum has failed to model the bone properly and the normal trumpet-shape of the end of the shaft is distorted and often lost Occasionally exostoses on the superficial and deep surfaces of an enlarged metaphysis may produce such irregularity in density of the radiographic shadow as to suggest cavitation of the bone and possibly lead to an erroneous diagnosis of dyschondroplasia.

Pathology—As already indicated two abnormal processes are concerned in diaphysial aclasis One or more fragments of cartilage from the margin of an epiphysial line becoming isolated on the surface of the metaphysis proliferate and form exostoses and the periosteum which is incomplete at the sites of these cartilaginous nests fails to model the metaphysis in a normal manner It was this periosteal failure which first suggested the word aclasis in the title

Histological examination—On section an exostosis is seen to consist of cancellous bone directly continuous with the parent bone the apex being covered with a cap of cartilage from which it grows and which merges with the thickened periosteum surrounding its base The cartilage cap is covered by a bursa which may become enlarged as a result of recurrent injury from an adjacent muscle or tendon. When an exostosis is large and shaped irregularly

like a cauliflower the cartilage instead of forming a smooth cap dips into all the crevices with the result that section shows an apparently indiscriminate mixture of bone and cartilage. In one case of multiple exostoses with excessively large outgrowths from the posterior surfaces of the upper ends of both tibiae and another of a solitary large exostosis growing from the neural arch of the fourth lumbar vertebra, the author found on section nodules of cartilage some of them calcified buried in the loose cancellous bone of the exostosis. This unusual finding does not, however seem to warrant the assumption that in such cases there was a combination of the two conditions diaphyseal aclasis and dyschondroplasia.

Progress and complications—Though an exostosis may enlarge slowly throughout the time that the shaft continues to grow the rate of growth of different exostoses in a multiple case seems to vary considerably Many show little if any change over a period of years, whereas *two or three may reach a size capable of causing inconvenience Occasionally one* will grow to a considerable size the enlarged head becoming irregular and even branched. Such changes usually occur in a solitary exostosis particularly if it is growing from the scapula or pelvis. In the vast majority of cases when growth of the skeleton ceases and the adjacent epiphysis fuses with the shaft the exostosis ceases to grow and the cap becomes ossified Occasionally however the cartilage on one of the exostoses may continue to proliferate and become so active as to form a rapidly enlarging chondromatous tumour On section foci of calcification and ossification may be found in the substance of the tumour Enlargement of an exostosis may be delayed for many years and then begin suddenly long after growth should have finally ceased. The rapidity with which there is increase in size of some of these chondromata, or osteo-chondromata as they often are naturally raises the question of possible malignant change Careful microscopic examination after biopsy or even of the whole tumour after it has been removed does not always settle the question with certainty Willis (1948) considers that the solitary exostosis— the commonest tumour of the skeleton —should be regarded as an osteoma and not simply as a solitary type of the multiple condition and he remarks that it is not unusual for it to develop a chondrosarcoma.

Geschickter and Copeland (1936) reported malignant change in 7 per cent. of 202 cases of exostosis but many of the cases they included do not appear to be examples of the condition which is now being discussed Jaffe (1943) in a small series of twenty-eight cases gave the frequency of malignant change as 11 per cent. There must of course be many cases of true exostoses which are seen by clinicians, and even operated upon, which never come to the knowledge of pathologists and it would seem wise at present, to admit that although the fact of occasional development of a chondro-sarcoma from the cap of an exostosis must *be accepted, the frequency of this complication is unknown* Some cases are undoubtedly malignant (Platt 1931 Gardner 1937) the bones most likely to be involved being the femur the scapula and the pelvis. It is not always easy to determine whether a large chondromatous or chondro-sarcomatous tumour has arisen endosteally or in the cartilage cap of an exostosis.

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CASE 29—DIAPHYSIAL ACLASIS

(Figs. 88 to 91) Woman twenty-one years of age Deformity of forearms noticed at the age of eleven years with some thickening of the fingers six months later There were large numbers of exostoses in the usual situations throughout the skeleton One metacarpal and a few phalanges showed small bone outgrowths. No material change seen in radiographs during the past eight years



Fig 88

Case 29—Forearms Note the shortening, curvature and pointed lower extremity of both ulnae and secondary curvature of the radii Small exostoses are seen near the lower ends of all four bones, and also at the upper ends of both ulnae—an unusual sit The difference in length of the two bones is also seen at their upper ends where it has disturbed the relative position of the trochlea and capitellum in both elbows



Fig 89

Case 29—Left leg, age thirteen years Short fibula with abnormal position of both ends, and striking enlargement of upper metaphyses Apparent fusion of the tibia and fibula, above and below is probably due to overlap of shadow



Fig. 90

Case 29—Right shoulder showing several exostoses of the sharp pointed variety directed towards the centre of the shaft. General want of modelling of the metaphysis is not very marked. An exostosis is seen on the second rib (a similar projection was seen on the corresponding rib on the left side so that the bone thickening may not be due to the attachment of the serratus magnus).



Fig. 91

Case 29—Right knee. The lower femoral metaphysis shows irregular enlargement, with loss of the normal trumpet-shape and with exostoses projecting from its surface. Note the characteristic shape of the exostoses which are inclined towards the centre of the shaft. An exostosis on the inner aspect of the tibial head appears to have been fractured.

SE 30—DIAPHYSIAL ACLASIS

g 9*) Adult male with exostoses
ecting both humeri at about the same
el, namely the mid-shaft—an unusual
ation

CASE 31—DIAPHYSIAL ACLASIS

(Fig 93) Specimen of the femur of a man aged about fifty years with a mushroomed exostosis growing from the lower metaphysis which shows little want of modelling



Fig. 92

Case 30—Humeri, showing sessile exostosis on the right and a pedunculated exostosis of characteristic shape on the left



Fig. 93

Case 31—Specimen in a man aged about fifty years.

CASE 32—DIAPHYSIAL ACLASIS

(Figs. 94 and 95.) Woman aged forty-seven years. She reported that she had sustained an injury to the left knee six months ago. The symptoms were regarded as being due to trauma, and not connected with the presence of exostoses which were principally in the region of the knee joints. Only one forearm was deformed.



FIG. 94



FIG. 95

CASE 32.—The left knee joint (Fig. 94) shows imperfect moulding of the femoral metaphysis with two minute exostoses. There are other exostoses arising from the tibia and fibula. There is evidence of an old fracture of the tibial spine. The left forearm (Fig. 95) shows marked shortening of the ulna, and deformity of the radius, with distortion and subluxation of the radial head. Note that the carpus is not materially tilted inwards by the radial deformity.

CASE 33—DIAPHYSIAL ACLASIS—with unusual features

(Figs. 96 to 98.) Male, aged eighteen years. Height 5 feet 7 inches. Lumps on legs were first noticed when he was twelve months old, thereafter gradually growing larger. No symptoms until recently. Complains of pain in the right thigh on walking. Twice in the last few months while cycling the right knee "clicked" and he was unable to bend it. On one occasion the knee locked in extension for a month, movement being regained gradually. Exostoses were present on most of the bones including the pelvis, clavicles, several ribs, phalanges, metacarpals and metatarsals. Even the os calcis in each foot was abnormal in shape, with an exostosis on the left. The enlargement of the upper part of the calves was enormous, even grotesque. The right ulna, and both fibulae, were short. Exostoses were removed from the right femur and both calves. The tumours in the calves were quite unlike the usual cancellous exostoses; they consisted of open-mesh bone with the spaces filled for the most part with mushy, gelatinous and mucoid material, containing here and there patches of cartilage and calcified cartilage.

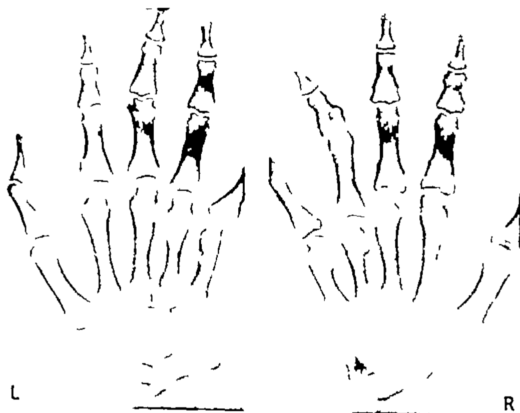


Fig. 96

Case 33—Hands showing small exostoses of several phalanges and some metacarpals. The left ulna is of normal length. The fourth metacarpal of the right hand is short.



Fig. 97

Fig. 97

Case 33—Antero-posterior view of the right knee and calf, showing that all three bones are affected The size and irregularity in density of the tibial growth is striking. The clear area in the tibia, sharply defined on one aspect, is rather suggestive of cavitation, but at operation this was disproved.



Fig. 98

Fig. 98

Case 33—Left knee showing an exostosis on the posterior aspect of the femur and an extraordinarily large outgrowth from the back of the tibia. Note the extensive attachment of the growth to the tibia, its nodular surface, and the great irregularity in density Part of the opacity is due to growth on the fibula.

CHAPTER 5

DYSCHONDROPLASIA

Synonyms—Ollier's disease Multiple enchondromata

Dyschondroplasia is a somewhat rare developmental error characterised by rounded masses or columns of unossified cartilage in the metaphyses and diaphyses of certain bones. It was first described and named by Ollier in 1900 An admirable review of the subject was published in 1935 by Hunter and Wiles.

It is often linked with diaphysial aclasis as pointed out in the section dealing with that affection the two conditions being regarded as variants of the same fundamental developmental error This may lead to confusion which is quite unnecessary though both result from a fault of the epiphysial line nests of cartilage becoming misplaced instead of being calcified and ossified in the normal manner they are radiologically and in other ways quite different and in the vast majority of cases are readily distinguishable In the condition to which the author prefers to confine the term dyschondroplasia, masses of cartilage are found inside the metaphyses, the lesions being essentially endosteal and not projections on the surface as are exostoses.

Hereditary and familial influences—These influences play no part in the incidence of dyschondroplasia as they do so commonly in diaphysial aclasis.

Sex—Both sexes are affected males rather more frequently than females (Stocks and Barrington 1925)

Age—The diagnosis is usually made in childhood in exceptional cases the shortness of an affected limb may be noticed at birth.

Etiology—The cause is unknown it is said to act between the fourth and eighth months of foetal life (Speiser 1925) but there seems to be no doubt that in many cases it must have been active at a later date. Bentzon (1924) pointed out that the columns showed a tendency to radiate towards the epiphysial line from the point of entry of the nutrient artery (*e.g* in the upper tibia) and he suggested that the cause might be hyperaemia due to anomalies of the vegetative nervous system A number of experiments were carried out to prove this theory but without convincing success.

Distribution—There is a strong tendency towards unilateral distribution of the lesions though seldom strictly so Enchondromata of one hand are commonly associated with a few enchondromata in the opposite hand, particularly in the thumb and little finger with or without one or two in other bones. Enchondromata may however be confined to a single bone or to some bones of a single limb. The two lower limbs only may be affected. In rare instances all four limbs show fairly extensive changes. The bones chiefly involved are the long bones formed in cartilage and as in the case of diaphysial aclasis it is at the more rapidly growing ends of these bones that the lesions are most often seen. The region of the knee joint and the lower ends of the radius and ulna are particularly common sites but enchondromata are quite common at the upper ends of the femur and humerus respectively and at the lower ends of the tibia and fibula. In the upper femur columns of cartilage radiating from the lesser trochanter are not uncommon. As in so many developmental errors the region of the elbow joint is singularly free from changes. The long bones of the hand and feet particularly the phalanges are favourite sites for numerous enchondromata which are frequently the cause of obvious and disabling deformities. Dyschondroplasia

differs markedly in this respect from diaphysial aclasis in which phalangeal exostoses are *few* and insignificant. The pelvis is a common site the scapula rather less so. The ribs, sternum and skull are seldom affected and the tarsus very seldom. The carpus and the spine usually escape but the sacrum in one of our cases was affected on both sides in addition to the ilium and pubis on one side. The middle part of the shaft of a long bone is seldom the site of lesions when this does occur it is usually but not exclusively in the most severe cases the occurrence of changes in the mid-shaft suggests that errors in development must have been active in foetal life ✓

Clinical signs—In typical cases the affected arm and leg are *dwarfed* to a varying degree sometimes they are grossly dwarfed. In a youth of eighteen years the affected lower limb was ten inches shorter than the other When one half of a metaphysis is occupied by columns of cartilage to a greater extent than the other the rate of growth at the corresponding half of the epiphysial line is often retarded. In this way *deformities* such as genu valgum may develop in addition to general shortening of the affected limb Deformity caused by large enchondromata in the phalanges is very common in extreme cases a hand may be practically useless. As in diaphysial aclasis and certain other affections the ulna frequently displays a greater degree of shortening than the radius in these circumstances the shaft of the radius may be curved, and occasionally the radial head is dislocated. There may be cubitus varus at the elbow and inward displacement of the hand at the wrist. Seldom is the radius the shorter of the two bones. The fibula may be shorter than the tibia without producing deformity of the latter bone. Facial asymmetry is sometimes present (Hunter and Wiles 1935) Involvement of cranial nerves, including the optic nerve was reported by Nielson (1941). Fractures are distinctly uncommon except in severely affected phalanges. *Blood examination* reveals no abnormality

Radiographic appearances—In the metaphyses radiographic examination reveals cartilage filled clear spaces of varying size and shape but with a marked tendency except in the hands and feet towards a columnar arrangement the columns extending a varying distance into the shaft of the bone. The density of bone between cartilage columns is often increased, and these intervening bony septa may give rise to a striated or streaky appearance in the affected metaphysis. There seems to be no sufficient reason, however for linking the condition of striated bones reported by Voorhoeve (1924) with dyschondroplasia and osteopoikilosis as suggested by that author The shaft of a major long bone with the metaphyses at both ends severely affected, besides being unduly short is often thick and dense Only rarely is the shaft of a major long bone extensively involved in such a case the mottled cyst like changes may give rise to difficulty in diagnosis and call for biopsy unless the hand or foot shows typical changes. An affected metaphysis may show little if any distortion of shape but in well marked cases some enlargement is usual and occasionally this is gross. Not infrequently there is curvature of the affected part of the bone particularly when the cartilage columns are confined more or less to one side of the metaphysis. When a metaphysis is distended by large masses of cartilage these often protrude through the cortex. A breach in the cortex may also be caused by a relatively small column of cartilage this may be seen not infrequently in a shaft some distance from the epiphysial line. If more than a nipple-like projection is formed, the gap in the cortex is often limited on one side by a sharp bony point which may be mistaken for an exostosis. Cortical projections formed in this way point towards the epiphysial line whereas true exostoses are always inclined in the opposite direction towards the centre of the shaft. Occasionally a small islet of cartilage is seen lying *in* the cortex of a long bone The way in which normal growth and modelling of a metaphysis may cause protrusion of an enchondroma which was originally completely endosteal and which has not materially increased in size is well illustrated by Langenskiöld (1947) Though enchondromata and exostoses may be associated occasionally in the same case

we believe that this combination is very rare indeed and in fact much more rare than some authors would have us believe In younger children the epiphyses usually show no abnormality but in older children even from five years upwards according to Hunter and Wiles irregularity in density with mottling and occasionally streaking of some epiphyses may be seen. In one of our cases dense mottling of several epiphyses was a striking feature in films taken before the age of three years. These epiphysial changes are not uncommonly confined to half an epiphysis and are never seen unless the corresponding part of the metaphysis is the seat of definite changes. In the adult abnormal streaking still visible in the shaft of a bone may be seen to extend into what was the epiphysis. In the digits distension and loss of continuity of the cortex over one or more chondromata is very common and the chondromata may occur anywhere in the shafts of these bones showing much less preference for the metaphyses and no tendency to a columnar arrangement. The commonest site in the pelvis is the ilium near the crest though chondromata may be seen in the pubis or ischium. The typical appearance in the ilium is that of clear columns radiating in a fan-like manner towards the crest. In two of our cases, both ilia were affected.

In older children and adolescents dense spots are seen scattered throughout an affected metaphysis and even in the adjacent epiphysis or part of it. There is loss of definition of the cartilage columns and a general suggestion of ossification and healing this transformation is usually well advanced by the time skeletal growth has ceased. According to Hunter and Wiles (1935) these changes are seldom seen till after six years of age. Dense spots found in a child of two and a half years (Figs. 106 to 108) appeared at an exceptionally early age. Though such dense spots are found in enchondromata in the fingers the tendency to arrested growth and to ossification is much less evident in these bones than in the major long bones.

Progress and complications—As a rule there is little tendency except in the hand and foot, for the masses of misplaced cartilage to proliferate. In the fingers the presence of many enchondromata of considerable size fungating through the cortices may eventually cause complete crippling of the hand. In a man of thirty-two years the total width of the fingers in a completely useless hand amounted to seven and a half inches. As already indicated, there is usually little tendency for the cartilage columns to calcify and ossify before adolescence is approached. In a major long bone proliferation of an endosteal nest of cartilage occasionally continues after growth has ceased, but this is very unusual. Even more rare is the development of a chondro-sarcoma. It is not always easy to determine whether such a growth has arisen endosteally or started in the cartilage cap of an exostosis the latter appears to be distinctly the more common of the two. The upper part of the humerus and the pelvis are sites at which chondro-sarcomata of apparently endosteal origin have been reported. Excessive enlargement of a mass of misplaced cartilage except in the digits is more common when the mass is solitary Willis (1948) considered that a solitary chondroma like a solitary exostosis or osteoma should be regarded as a neoplasm and not as an isolated result of the developmental error we are discussing here.

Pathology—Histologically the masses consist of hyaline cartilage with cells of varying size some abnormally enlarged, arranged in a somewhat irregular manner There may be septa of fibrous tissue Calcification and ossification of the cartilage may be seen, particularly in older patients In the larger chondromata signs of degeneration may be evident

Diagnosis—Advice is usually sought because there is deformity Radiographic examination then reveals the true nature of the case. The interpretation of radiographs of a single bone particularly in adults may be very difficult the appearances may be misleading But when all the radiographic evidence is examined the diagnosis is usually easy Films of the digits are particularly helpful in doubtful cases. In osteopoikilosis the dense spots in metaphyses and epiphyses which are a feature of the condition are not confined to two limbs as is so often the case with dyschondroplasia moreover in that condition, apart from the spots the

bones are normal in density and outline. Only occasionally is biopsy advisable. Osteotomy for the correction of deformity when it is called for gives the surgeon an opportunity to confirm the diagnosis. After osteotomy the fragments unite readily

MAFFUCCI'S SYNDROME (1881)

This is a condition in which dyschondroplasia is associated with cavernous haemangiomata and phleboliths in the soft tissues. Carleton *et al.* (1942) gave an admirable review of the twenty cases published in the literature and reported two cases of their own. In the first of these a group of phleboliths was seen in relation to irregular enlargement of the anterior surface of one tibial shaft. Except in this case and one published by Krause (1944) in which all lesions were confined to one side of the body the bone and soft tissue lesions seem to be entirely independent in their distribution

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CASE 34—DYSCHONDROPLASIA—Both lower limbs

(Fig 99) Girl aged four and a half years. Left leg bowed due to deformity of the femur and all major long bones of the limb shorter than on the right. Arms and hands not affected. Enchondromata in the right ilium—very slight (and none at all in the left ilium) and at the ends of the femur tibia and fibula of both lower limbs the changes being much more marked in the left Though the distribution of lesions is unusual this case shows particularly well the columnar arrangement of changes in the metaphyses (Under Dr Donald Paterson)



Fig 99

Case 34—Lower limbs showing characteristic changes in the metaphyses The tendency to columnar arrangement of the cartilaginous masses is well shown Irregular density and mottling are seen in several epiphyses Note that only the inner half of the epiphysis of the right femur is mottled and only the inner half of the metaphysis contains columns of cartilage

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CASE 35—DYSCHONDROPLASIA—Almost completely unilateral

(Figs. 100 to 103.) Male. Shortness of the left arm and leg noticed at birth. No other members of a large family affected. When seen in 1925 at the age of twelve years (then under the late Dr Gordon Pugh) there was marked shortening of the left arm and leg. Enchondromata were visible on the left side in the lower angle of the scapula, both ends of humerus, lower ends of radius and ulna, hand (numerous), ilium, both ends of femur, upper ends of the tibia and fibula, and long bones of the foot. On the right side cartilaginous nests were seen only in the ilium and the little finger. Lesions in the major long bones showed typical columnar arrangement with already a few dense foci of calcification and ossification in some metaphyses. In 1946, at the age of thirty-three years, he was again seen when in the care of Mr J. S. Batchelor. Shortening of the affected limbs was marked. Dense mottling and loss of definition of the lesions, indicative of attempts at "healing," were most striking when the films were compared with those taken in 1925. This change was most obvious in the metaphyses of the major long bones, but there were many intensely dense spots in the enchondromata of the left hand which was grossly deformed and practically useless; it measured seven and a half inches across the fingers. Lesions were then visible in the right thumb and lower end of the right radius. All other lesions had been recognised twenty-one years earlier. (Reported by Fairbank, H. A. T. (1927) British Journal of Surgery, 15, 120, and Rae, J. L. (1936) Proceedings of the Royal Society of Medicine, 29, 1663.)



Fig. 100

Case 35—Left forearm at the age of twelve years, showing typical endosteal cartilaginous columns deforming the metaphyses of both radius and ulna and irregularity in the density of their respective epiphyses. The bones are short, thick, and strong—the ulna, as usual, being the shorter of the two. Only a few dense spots of ossification are visible in the affected part of the radius. Note that the carpus is unaffected.



Fig. 101

Case 35—Left knee at age of twelve years, showing gross changes indicative of dyschondroplasia in the metaphyses of all three bones. Typical columnar arrangement of the cartilage masses is well seen in the tibia. Dense spots of ossification are visible in the femur. The epiphyses of the two major long bones are not affected but that of the fibula is somewhat mottled. What appears to be a small exostosis is seen on the inner side of the tibia.



Fig 10*

Case 35—Hands at the age of thirty two years showing enchondromata in every bone of the left hand, with innumerable dense spots of calcification. The lower ends of the radius and ulna appear to be healed. In the right hand there are enchondromata only in two digits and their corresponding metacarpals. The lower end of the right radius is deformed but there is no change on which a diagnosis could be made with certainty.



Fig. 103

Case 35—Pelvis at the age of thirty three years showing "healed" lesions in both ilia, the left pubis and the left great trochanter



Fig. 104



Fig. 105

Case 35—Fig 104 shows the left knee at the age of thirty-three years there is great advance in ossification of the cartilage masses compared with the film taken at the age of twelve years (Fig 101) Fig 105 shows the left ankle and foot at the age of thirty three years there are densely calcified spots in the lower ends of the tibia and fibula and in the phalanges The tarsus shows changes which are not characteristic of any particular dysplasia

CASE 36—DYSCHONDROPLASIA—Bilateral to a greater degree than usual all four limbs markedly affected

(Figs. 100 to 108) Girl. One other child, a male died of hydrocephalus at the age of three years. First observed when seven months old. Deformities have progressed steadily ever since and are now gross at the age of two years and eight months. (Under Mr R. G Pulvertaft)



FIG. 108

Case 36—Pelvis at the age of two years, showing typical radiating columns of cartilage near the crests of both ilia, and enchondromata in both ischia, right pubis and both femora



Fig. 107

Case 38—Hand at the age of two and a half years showing numerous typical enchondromata in both extremities to an approximately equal extent. The multiple dense centres of ossification in the cartilage at the lower end of the right radius and both ulnae is most unusual at this early age and gives an appearance not altogether unlike that seen in dysplasia epiphysealis punctata. Note that the shafts of the radii and ulnae are short and stout, the ulnae being as usual more shortened than the radii.

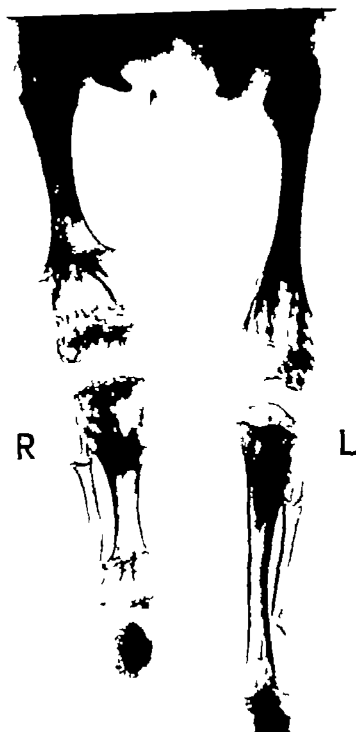


FIG. 10[illegible]

Case 3[illegible]—Lower limbs at age of two years eight months showing all six major long bones affected with shortening of the right lower limb. Stippling with dense ossific centres in the epiphyses and adjacent metaphyses, the latter largely cartilaginous, is a striking feature and is a most unusual appearance at this early age. Similar stippling can be seen in the right tarsal bones. Note the spikes formed by the cortex at the lower end of the shaft of both femora. In left leg the fibula is more affected and much shorter than the tibia.

CASE 37—DYSCHONDROPLASIA

(Figs. 109 to 111.) Male aged seventeen years. Right arm and leg affected. Gross interference with function of hand due to size and number of cartilaginous tumours. Particularly severe deformity of the leg. (Under Mr McCrae Aitken.)

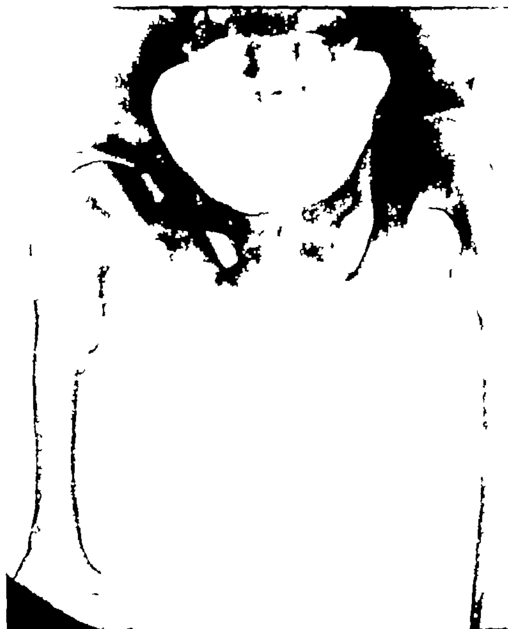
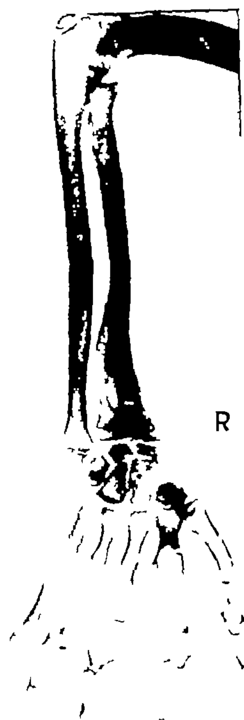


Fig. 109

Case 37—Pelvis and femora showing typical changes in the shortened right femur. The considerable involvement of the shaft and the texture of the bone, particularly of the lower metaphysis, are unusual.


R


R

CASE 38—DYSCHONDROPLASIA—Incompletely unilateral distribution

(Fig 112) Male aged eighteen years. Right arm and leg markedly short and deformed. Never had osteotomy performed. Right leg ten inches shorter than left due partly to deformity of femur and tibia. Unusual features were enchondromata in left pubis as well as in both ends of left fibula and *both* ends of the right ulna with dislocation of the right radial head. There were a few enchondromata in the left thumb and little finger and many in the right hand. (Under Mr H. H. Langston.)

CASE 39—DYSCHONDROPLASIA—Unilateral case

(Fig 113) Boy aged eleven years. Left upper limb and left lower limb very short. Bones of both these limbs contain many enchondromata which are particularly numerous in the left hand. Sacrum and left pubis are clearly affected as well as the left ilium. Upper metaphysis of the left humerus and both ends of the left femur show extensive changes. Dense spots of calcification and ossification are present in many of the cartilaginous masses; they are particularly numerous and closely packed at the upper end of the humerus. (Under Mr L. W. Plewes.)



Case 38 —F[illegible] shortening and the dislocation

CASE 40—DYSCHONDROPLASIA—affecting left forearm only

(Fig 114) Male aged nine years. Noticed deformity for three years. Recently complained that the arm pained him when working in the gymnasium The lump was said to be increasing in size. Definite cubitus varus with some prominence of the head of the radius. Left forearm one inch shorter than the right Pronation limited by a quarter supination free Bony prominence on the front of the lower third of ulna. Humerus not shorter than right. No exostoses felt on any bone No radiographic changes found except in this limb.



Fig 114

Case 40—Shortened ulna with curious appearance and spots of calcification in the clear area in the head of the bone Radius curved Typical enchondromata in third finger confirmed the diagnosis.

CASE 41—DYSCHONDROPLASIA—Atypical case

(Figs 115 and 116) Male aged fourteen years Progressive limp in the right leg had been noticed since the age of four years Four fractures had occurred in the shaft of the right femur in the last six years There was café-au-lait pigmentation over the upper dorsal and lower lumbar regions of the spine Total shortening of the right lower limb was no more than half an inch but this was because gross shortening of the right femur was compensated by lengthening of the right tibia and fibula. Biopsy of the right tibia was followed by a pathological fracture and later by fusiform enlargement of the shaft of the bone Microscopic section showed only cartilage cell Blood examination revealed no important abnormality Well-marked though very atypical changes were seen in the right femur and tibia. Lesions which though atypical might have been enchondromata were also seen in the upper half of the shaft of the left humerus the lower end of the shaft of the right ulna in some phalanges of both hands in the right ilium near the crest both fibulae the trochanteric region of the left femur and possibly in the shaft of the left tibia. There was one spot of irregular decalcification in the centre of the left parietal bone seen in the antero-posterior radiograph of the skull. The distribution of lesions in the lower limb was not metaphysial but biopsy suggests strongly that this case should be classified as dyschondroplasia. (Under Sir Harry Platt and Mr A F Brewon.)





Fig. 115 Fig. 116

Case 41.—The right femur (Fig. 115) shows various mottled appearance in the lower two-thirds or more of the shaft and an old united fracture in the middle third of the shaft. The right leg (Fig. 116) shows unusual changes affecting most of the shaft of the tibia with fusiform enlargement at the site of a pathological fracture which occurred after biopsy. Somewhat similar changes, certainly not typical of dyschondroplasia, are seen in the upper and middle part of the shaft of the fibula.

METAPHYSIAL DYSOSTOSIS

In this excessively rare condition the metaphyses of all long bones consist for the most part of unossified cartilage. The radiographic appearances are unique and they differ considerably from those seen in dyschondroplasia.

In 1934 Murk Jansen of Leiden published a case. Seven years before he had presented a set of radiographs of the patient, who was then five years of age, to the Royal College of Surgeons of England. By courtesy of Sir Arthur Keith, formerly Conservator of the Hunterian Museum, the author was able to secure prints of all the films. Search of the literature has failed to disclose a single comparable case.

The patient was a boy, born with club feet which were treated by manipulation. The ankles and the lower ends of the radii and ulnae gradually thickened. The child crawled at six months, but he was unable to walk at three years. Eventually, however, he succeeded in walking with the help of splints. He was dwarfed, and at ten years of age was at least twelve inches below normal height. The lower limbs were more affected than the upper limbs, and they were markedly deformed. The feet were valgoid. The skull and spine were normal. Dentition was somewhat delayed. At five years there was some anaemia, and the serum calcium was high (16.0 mg.) but this gradually came down to 13 mg. per cent. Other investigations of the blood and urine were negative. At ten years further investigations revealed no abnormality. Jansen considered that the cause was abnormal intra-uterine pressure acting at a particular stage of foetal development, a theory which he postulated in the explanation of other developmental errors.

Radiographic features—The epiphyses have developed remarkably well and are of normal density, but the metaphyses both at five years and ten years of age are still cartilaginous and irregular, cloudy and impregnated with salts. Some of the epiphyses are displaced from the lines of the shafts. This is more obvious in films taken at the age of five years than later. The shafts of the long bones are stout, many are curved, and they end very irregularly with some expansion. There is a wide interval between shaft and epiphysis, the space containing a varying number of rather dense and discrete centres of ossification, especially close to the shaft. There is no suggestion of a columnar arrangement of the cartilaginous metaphyses as in dyschondroplasia, and the epiphyses are not mottled either partly or wholly, as they may be in the allied condition. The spots of calcification and ossification in the metaphyses vary in size, shape and density, and they are not quite like the circular dense spots which are seen in the "healing stage" of dyschondroplasia. Many of the metaphyses appear to be enlarged. Changes in the hands differ strikingly from those of dyschondroplasia; the cartilage masses, dotted with fragments of bone, are seen only adjacent to every epiphysis and they are not distributed irregularly as isolated enchondromata anywhere in the shafts of the metacarpals and phalanges. The carpus and much of the tarsus seem to be ossified normally, but the posterior part of the os calcis shows changes similar to those in a metaphysis. At the age of five years, but not at ten years, irregular or punctate ossification is seen in the navicular and cuneiforms. In the pelvis the anterior parts of the ilia are mottled, but there is no such mottling as one might have expected in the bone near the crests. The skull, spine, ribs and clavicles appear to be ossified normally.

Pathology—A fragment from the lower end of one tibia, including portions of the shaft and the cartilaginous metaphysis, was examined histologically. "The cartilage cells were either small and collected into nests or large and myxoedematous." Calcification was seen in the matrix. The junction of diaphysis and cartilage was irregular, and isolated masses of bone were seen in the substance of the cartilage, "as in rachitis."

Note. Two cases have been brought to our notice by Dr. Norah Walker and M. G. M. Müller respectively which, though by no means strictly comparable with Jansen's case, certainly show widespread metaphyseal dysplasia and do not appear to belong to any other recognised group.

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Fig. 118 Fig. 117

M... dysostosis

...—The boy ... ten years, showing deformities ... lower limbs ... of the right shoulder ... upper arm ... the unossified cartilaginous metaphyses ... end of the ... centres of ossification at the upper end, and ... epiphy... the dwarfing ... twelve inches below



Fig. 119

Case 42—Hands at the age of ten years showing the changes not scattered throughout the shafts as in dyschondroplasia but concentrated almost entirely in the metaphyses. Not that the carpal bones are unaffected.

Fig. 120

Case 42—At the age of five years showing irregular ossification of the anterior part of the ilia and the acetabula and the stout curved femora with expanded upper extremities and largely unossified necks.



FIG. 121

Case 42—Ankles and feet at the age of ten years showing very irregular ossification and deformity of the lower metaphyses of tibiae and fibulae. Note well formed epiphyses of these bones and irregular ossification of posterior part of the os calcis in both feet.

FIG. 122

Case 4? Knees at the age of 6 years showing the stout femora, the unossified metaphyses with mottled centres near the diaphyses and the well-ossified epiphyses of both the femora and tibiae. Note the displacement of the upper tibial epiphyses.

(Figs. 117, 119 and 121 are taken from Dr Jansen's article.)

FAMILIAL METAPHYSIAL DYSPLASIA

In 1937 under the above title Bakwin and Krida reported two cases a boy of eleven years and his sister of nearly seven both affected by a condition the feature of which was symmetrical enlargement of one or both ends of the shafts of the long bones. In 1931 Pyle had reported the boy as a case of Unusual Bone Development. These two were tall, slender long-legged children apparently in perfect health. Both had genu valgum and limited extension of the elbows The enlargements affected a third or more of the shaft extending from the epiphysial line a varying distance before fading off to the normal—possibly subnormally slender—middle third of the shaft. The enlarged portions were of uniform low density with little sign of a cortex. The epiphyses were normal. The unaffected portions of the shafts were rather more slender than normal and a little more dense both these features being exaggerated by the enlargement and translucency of one or both ends of the shafts In the femora the lower halves of the shafts were chiefly involved the upper much less so Both ends of the tibial shafts appear to be enlarged the upper more than the lower The proximal ends of the humeri the distal ends of the radii and ulnae and the inner ends of the clavicles were affected. The metacarpals and possibly the ribs showed slight changes. The condition showed no indication of being progressive Except for some relative lymphocytosis the blood was normal. Pyle performed an osteotomy for genu valgum and found the femora abnormally soft union took place normally There seems no doubt that the condition is the result of a congenital developmental error The appearance of the bones in the radiographs is somewhat similar to that seen in two brothers reported by Ellis (1934) as cases of osteopetrosis In them the abnormal density of the middle portions of the long bones was much more definite Bakwin and Krida refer to a report by Ingalls (1933) on museum specimens of dry femora and tibiae which showed similar symmetrical enlargement of the lower halves of the former and the upper halves of the latter The medullary cavities were very short and confined to the narrow parts of the shafts. These bones were obtained from a tall thin man who died of tuberculosis.

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CASE 43—FAMILIAL METAPHYSIAL DYSPLASIA

(Figs. 123 and 124) Male aged five years. Taken to hospital for genu valgum. Perfectly healthy child. Head a trifle large and frontal prominent Ends of shafts of all long bones felt abnormally large. Slight limitation of extension of elbows. Radiographs showed enlargement of ends of the shafts with very thin cortices the middle thirds or less, of the shafts were of normal size with normal cortices. Osteotomy of the femora for correction of the genu valgum showed the bone abnormally soft. No excessive bleeding Union occurred normally (Pyle 1931)

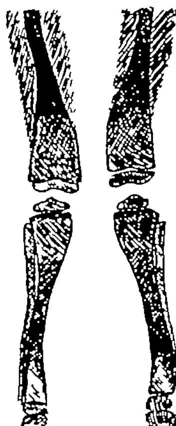


Fig 123



Fig. 124

Case 43 Figure 123—Legs showing the abnormal shape and structure of the bones Figure 124 shows similar changes in an arm, particularly in the radius (After Pyle)

CHAPTER 8

DYSPLASIA EPIPHYSIALIS MULTIPLEX

This is a rare congenital developmental error characterised by mottling or irregularity in density and outline of several of the developing epiphyses, dwarfism and stubby digits. In 1934 Jansen published, under the title of "Epiphysial Dysostosis," a case which we consider belongs to this group. In 1935 the present author briefly called attention to the condition and the points in which it differs from dysplasia epiphysialis puncticularis (now punctata). In 1946 and 1947 we published further papers on a series of twenty cases of what we believe should be regarded as a clinical entity and suggested the above title. None of these cases had been published, but only two under the above title. In our opinion some at least, and possibly most, of the cases that have been published as examples of multiple osteochondritis belong to this group. We now have for study some twenty-six cases.

Hereditary and familial influences are not in evidence as a rule, but one case apparently inherited it from his mother, and two sisters and also twin brothers are included in our series.

Sex—Both sexes are affected, males more frequently than females.

Age—The age at which the developmental error was recognised varied from eighteen months to fourteen years, with two exceptions—a girl of twenty and a middle-aged woman. One case has been followed till over forty years of age.

Etiology—The cause is entirely unknown.

Distribution—The number of epiphyses affected varies from a few to all the major epiphyses, the most prone to show typical changes and permanent deformity being those at the hips, shoulders, ankles and rather less frequently the knees, wrists and elbows. The metacarpal and metatarsal heads and the phalangeal epiphyses show changes in some cases. The tarsal and carpal bones may be irregular in shape.

Signs and symptoms—Difficulty in walking has led to several cases being taken to hospital; in others the complaint has been of pain and stiffness in the knees and hips. In the older cases, as one would expect, arthritic symptoms are troublesome at times. Some degree of dwarfism of the short limb type was present in most of the cases. The face is bright and intelligent; signs of cretinism are absent. Enlargement of the epiphyses is occasionally seen. The hands are striking, the digits being short, thick and stubby with blunt ends, the relative length of the digits being normal in most cases. Apart from the short stature and the hands there is no suggestive deformity. In certain joints there may be laxity of ligaments and in others limitation of movement. Flexion deformity of the knees was found in a few cases. In one case the elbows were flexed and there was laxity of the wrists and knees. In another the elbows showed curious deformity with the radial heads subluxated. In yet another, a particularly severe case, there was limitation of abduction of the shoulders and of extension of the elbows, while the knees were flexed and the tibial heads subluxated backwards. Genu valgum, dislocation of the patella, and bow-legs were present in some. In Jansen's case (1934) a lad of thirteen years, both hips were flexed, the knees flexed and valgoid and the feet in the varus position. The spine is usually normal in length and ossification. Jansen's case was exceptional as there was marked platyspondyly with flattening and gross irregularity in outline of the vertebral bodies, and we have seen one other case in which the vertebral bodies were somewhat shallow and spread. Blood examination has given normal results.

Radiographic appearances—The essential abnormalities are seen in the epiphyses. The centres of ossification for these may be late in appearing and backward in development, and fusion with the shafts may be delayed, but the principal change is irregularity in ossification. The centres are irregular both in density and shape, being mottled and often mulberry like

in outline. Separate subsidiary centres around the main centre are common resulting in some peripheral stippling but this is never as complete as is seen in the punctata type of epiphysial dysplasia. There is a definite tendency towards improvement whatever the stage of development that happens to be under observation in contrast to osteochondritis in which the early changes become progressively worse before improvement commences. An affected epiphysis eventually becomes normal in density but the outline though usually but not invariably smooth remains permanently abnormal. The age at which this permanent deformation becomes apparent seems to vary considerably in different cases. Any or all of the epiphyses may be affected the typical changes and permanent later deformity being seen most frequently at the hips shoulders ankles and less commonly the knees. The femoral and humeral heads remain permanently shallow and less convex than the normal. In one exceptional case a girl of eight years the femoral and humeral heads had already assumed a smooth flattened shape and uniform density On the other hand in another typical case the femoral heads at the age of twenty-seven years still showed irregularity in outline and, on one side partial fragmentation a condition that in a younger patient might well be mistaken for pseudo-coxalgia which was in fact the faulty diagnosis made when he was first seen at the age of fourteen years. The great trochanters may also show changes. The femoral necks may or may not be thickened Irregularity in the shape of the acetabula is exceptional, though naturally modification of the shape must occur eventually to conform to the abnormal femoral heads. The same is true of other affected joints. The femoral condyles may show little more in the way of irregularity in ossification than is met with occasionally in normal children in whom some irregularity in outline and separate points of ossification may be seen most frequently at the back of the condyles. In some cases the faulty ossification is much more marked. In older children with ossification of the condyles approaching completion striking alterations in shape may be seen In some the condyles are flattened and inclined to be rectangular The head of the tibia may still show gross irregularity and mottling on one or both sides. In a case with particularly gross changes in all the epiphyses there was posterior subluxation of the tibial heads at sixteen years ossification was practically complete but the articular surface of one tibia was tilted forwards more than 45 degrees from the horizontal The patella may show definite mottling In one case the fibula was elongated the head lying unduly high The ankles show changes which if marked are of some diagnostic value The lower tibial epiphysis diminishes in depth from within outwards to an exceptional degree the joint surface is oblique the astragalus is altered in shape to conform to this and it may or may not be tilted outwards in addition. This deformity of the ankle joint was present in at least half the cases In three cases the external malleolus was abnormally low lower than the tibial deformity would account for The radius and ulna do not show a similar irregularity in length an exception was the case reported by Wiles (1033) in which the radius was relatively long The humeral head, in which changes are usually well marked and the fragmentation is gross sometimes appears to overlap the neck on the inner side to a striking degree while some flattening of the head as already stated is the usual final result Occasionally the permanent distortion is much more striking (Fig 140) Though the epiphyses in the neighbourhood of the elbow and wrist show irregularities of varying degree no permanent deformity of importance has been seen with one exception the case with subluxation outwards of the radial heads. In three cases the capitellum showed a poorly calcified ossific centre irregular in outline with a sharply defined nucleus of much greater density within it

The metaphyses may be trumpeted with the epiphysial lines irregular but they show no consistent or characteristic change The shafts of the long bones are often shorter than normal but are only exceptionally thickened In two cases the upper portions of the humeral shafts were enlarged, with trumpeting of the ends and grossly deficient ossification of the heads, the appearance being rather suggestive of the punctata group no other bones showed

a similar change The carpal and tarsal bones ossify late and may be very irregular in outline The metacarpals metatarsals and phalanges are stunted and their epiphyses may show irregular ossification Occasionally the metacarpals are rather suggestive of the Morquio-Brailsford type of chondro-osteodystrophy With two exceptions the cases in which the vertebral bodies were shallow and spread the spine has shown no changes. The skull and teeth are normal.

Progress and complications—As already stated the tendency is towards the normal, at least as regards density and texture but the shape of the epiphyses usually remains abnormal. Arthritic complications are almost inevitable sooner or later at least in the lower limb unless the residual deformities of the joint surfaces are comparatively slight.

Pathology—We know of only one histological study having been made of an epiphysis in an unquestionable example of this condition In a case under Mr J P Campbell a fragment of the upper tibial epiphysis showed Bone not very abnormal except that its bone corpuscles are rather scarce and in substance it is more of the woven bone type than compact Haversian, and Cartilage irregularly placed in the bony field definitely hyaline and perhaps tending to be softer and more mucinous than normal. Jansen (1934) published a microphotograph which appeared to show mucoid degeneration but this was of the metaphysis at the lower end of a femur not the epiphysis.

Diagnosis—When the signs of bilateral pseudo-coxalgia are found in a patient below the average in height it is advisable to have radiographs taken of other joints, *e.g* the shoulder and ankle, to exclude the presence of a generalised epiphysial dysplasia. Besides osteochondritis there are at least seven other conditions in which epiphyses may show irregular ossification Cretinism may be recognised by the typical facies dry skin, skimpy hair mental retardation stubby fingers which are approximately of equal length and the response to suitable treatment Delay in fusion at the epiphysial lines in cretins is associated with a band of sclerosis in the terminal layer of the metaphyses. Flattening of the humeral heads strikingly similar to that seen in epiphysial dysplasia was found in a cretin of thirty nine years (Berard and Novel 1930)

In dysplasia epiphysialis punctata the whole of an epiphysis appears to be ossifying from a number of discrete centres. The shafts of the long bones are short and thick, and the ends may be enlarged or splayed. The tarsal bones may be completely stippled showing nothing but a collection of dots. The abnormalities generally are much more gross than in the multiplex group. Congenital cataract occurs in about half the cases. In the Morquio-Brailsford type of chondro-osteodystrophy but not in gargoylism as a rule the femoral heads show striking epiphysial changes but in this condition the acetabula are markedly enlarged and irregular Other epiphyses and the carpus and tarsus often show some irregularities but the spine exhibits special features namely the shape of the bodies and in many cases angular kyphosis The central prolongation of the bodies—the forward projecting tongue—is quite distinctive and diagnostic. In dyschondroplasia the changes tend to be unilateral, and the irregularity or mottling is often confined to half the epiphyses and is never seen unless the corresponding portion of the metaphysis contains masses of unossified cartilage the epiphysial changes are comparatively insignificant and are entirely overshadowed by the metaphysial changes.

In osteopoikilosis the epiphyses are of normal shape and whether ununited or fused to the shafts show large numbers of the characteristic discrete dense spots which are not confined to the epiphyses. In osteopetrosis or marble bones occasionally some epiphyses show irregularity in density or are seen to have dense centres surrounded by less dense bone but the changes in the shafts dominate the picture Finally mottled epiphyses have been described in association with pituitary gigantism (Traub 1939)

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CASE 44—DYSPLASIA EPIPHYSIALIS MULTIPLEX

(Figs. 125 to 128) G H male, aged twelve years. Dwarfed. Grew one and a half inches in following year—? spontaneous or due to treatment with radiostol. (Under Dr H Gardiner Hill)



FIG. 125

Case 44—Wrist showing gross irregularity in shape and density of epiphyses of radius and ulna and abnormal shape of the carpal bones.



FIG. 126

Case 44—Hips showing retardation and irregular ossification of femoral head and great trochanters.

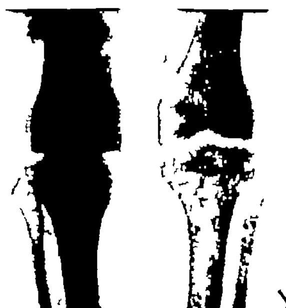


FIG. 127

Case 44—Knees showing curious angular shape of femoral condyles and irregularity of ossification of the inner tuberosities of the tibiae.

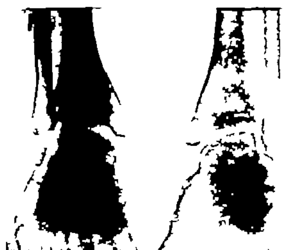


FIG. 128

Case 44—Ankles showing deformity of the lower tibial epiphyses and corresponding alteration in shape of the astragali

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CASE 44—DYSPLASIA EPIPHYSIALIS MULTIPLEX

(Figs. 125 to 128.) G. H., male, aged twelve years. Dwarfed. Grew one and a half inches in following year—? spontaneous or due to treatment with radiostol. (Under Dr H. Gardiner Hill.)

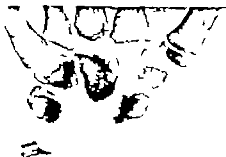


FIG. 125

Case 44—Wrist showing gross irregularity in shape and density of epiphyses of radius and ulna and abnormal shape of the carpal bones.

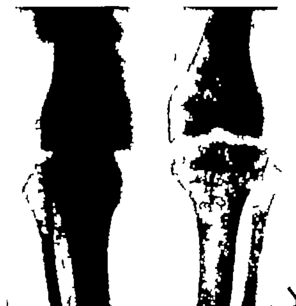


FIG. 127

Case 44—Knees showing curious angular shape of femoral condyles and irregularity of ossification of the inner tuberosities of the tibiae.



FIG. 128

Case 44—Ankles showing deformity of the lower tibial epiphyses and corresponding alteration in shape of the astragali

CASE 46—DYSPLASIA EPIPHYSIALIS MULTIPLEX

(Figs. 133 to 136.) G. B., male, aged eleven years. Advice sought, without result, from two hospitals for delay in walking in infancy. Difficulty in walking is still the trouble. Markedly dwarfed, of short-limbed type. Height at thirteen years 44½ inches (normal 57 inches). Intelligence normal. On standing marked lumbar lordosis with varus of one knee and valgus of the other, neither present when recumbent. Phenomenal degree of laxity of ligaments of some joints. Right hip, shoulders and elbows show some limitation of movement. Feet very flat. Fingers short and stubby. Radiographs show particularly severe errors in the ossification of all epiphyses and of the carpal and tarsal bones. The upper ends of the humeral shafts are enlarged and trumpeted, not a marked feature in the other major long bones. Femoral necks broad with marked changes in the femoral heads and acetabula. The skull shows some digital markings. (Under Mr. Eric Lloyd and Mr. D. Trevor.)



FIG. 133



FIG. 134

Case 46—Fig. 133. Elbow showing imperfect and fragmentary ossification of the epiphyses of all three bones. Fig. 134. Hand showing the short fingers, approximately equal in length (an unusual feature), the abnormal shape and texture of most of the bones, particularly the carpals, and the irregular shape of the epiphyses.



FIG. 135



FIG. 136

Case 46—Fig. 135. Ankle showing mottled ossification of the tibial and fibular epiphyses and the grossly abnormal shape of the astragalus. Note the oblique distortion of the tibial metaphysis. Fig. 136. Foot showing the irregular shape of the tarsal bones and unusual ossification of the apophysis of the calcaneum.

CASE 47—DYSPLASIA EPIPHYSIALIS MULTIPLEX

(Figs. 137 and 138.) J P female aged eight years. Admitted for swollen ankle and painful left knee. Femur had been osteotomised but this was eighteen months before Rather small well-proportioned girl, except fingers which are typically short and thick Left genu valgum knee very stiff and sensitive. Shoulders and hips show some limitation of abduction Elbows show curious deformities with internal epicondyles prominent and displaced forwards the radial heads displaced (left outwards right backwards and outwards) with separation of the radius and ulna. Mentally normal. Radiographs showed widespread changes in the epiphyses the changes affecting the shape rather than the texture. The epiphyses tend to be flattened and shallow and resemble the final stages seen in some other cases of moderate severity though the child was only eight years old



FIG 137

Case 47—Shoulder showing th flattened shallow h meral head, without changes in texture



FIG 138

Case 47—Hips showing shallow femoral heads, of normal density without obvious cha ges in the acetabula, and only slight enlargement of the femoral necks

CASE 48—DYSPLASIA EPIPHYSIALIS MULTIPLEX

(Figs. 130 to 149) J S female aged thirteen years. Complained of aching pain worse after exercise in both knees for past two and a half years. Not able to climb jump or run No swelling Parents and two siblings normal. Rather stunted but otherwise normal. Costo-chondral junctions palpable and enlarged Some limitation of movement of shoulders and elbows. Carrying angle increased in both elbows Subluxation backward of the tibia in both knees, with limited extension Blood examination negative. Osteotomy performed piece of upper epiphysis of one tibia removed for section. Radiographs show particularly marked abnormal ossification of all epiphyses and the short bones. The fragmentation and stippling of the epiphyses is exceptionally severe and some of the metaphyses show splaying notably the upper tibial and upper humeral and many end in an irregular epiphysial line. At sixteen years, still considerable irregularity in epiphysial ossification in several bones but in some ossification is practically complete with a unique degree of distortion of the shape and disappearance of all mottling The shoulders and knees show this particularly well. (Under Mr J P Campbell.)



Fig. 139

Case 48—Elbow at thirteen years, showing delayed and abnormal ossification of epiphyses, and some splaying of the humeral metaphysis Note the curious ossification of the outer condyle a dense nucleus for the capitellum being surrounded by less dense bone

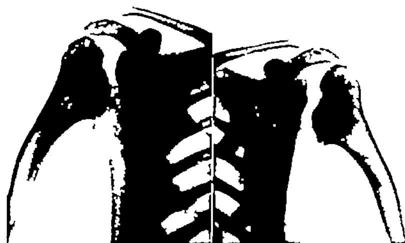


Fig. 140

Case 48—Shoulders at sixteen years showing exceptional degree of permanent malformation of the humeral heads and obliquity of the epiphysial lines



Fig 141

Case 48—Left knee at sixteen years, showing the severity of the permanent deformity of the femoral condyles and the upper end of the tibia.



Fig 14

Case 48—Ankles at sixteen ear showing the permanent deformity in both, with marked obliquity of the tibial articular surface and corresponding deformity of the astragalus.

CHAPTER 9

DYSPLASIA EPIPHYSIALIS PUNCTATA

Synonyms—Stippled epiphyses Chondrodystrophia calcificans congenita (Hunermann)

The chief characteristic of this rare disorder of infancy is the presence of a number of discrete centres of unusual density in many cartilaginous epiphyses and apophyses. Attention was first called to the condition by this author in 1927 two cases being reported briefly In 1935 he classified it under the title "epiphysial dysplasia puncticularis this being one of two which at his request were suggested by the late Sir Frederick Still. The alternative adjective punctata, which is no less descriptive and was also suggested independently by Dr Parkes Weber (see Bateman 1936) seems to be preferred in this country and it has therefore been adopted. Details of eight further British cases are now available, all but one of which have been published by various authors. Other cases have been reported under the title of stippled epiphyses but the published radiographs do not seem to justify their inclusion in this group Further search has disclosed an undoubted case reported by Conradi in 1914 under the title of chondrodystrophia foetalis hypoplastica. A few other cases have been reported in the literature of other countries the title favoured being chondrodystrophia calcificans congenita (Hünermann 1931) In all we have some sixteen cases for study

Hereditary and familial influences—There is no evidence of hereditary influence and seldom of familial influence in the incidence of this condition. *Sex*—Females are affected more frequently than males in the proportion of more than two to one.

Age—Fourteen cases were discovered within the first nine months and some within the first few days of post natal life. Only two cases were over two years of age one of these was alive at nine years. The dysplasia undoubtedly begins in foetal life.

Etiology—The cause of the condition is unknown.

Clinical signs—*Dwarfing* of the short limb type is usually if not invariably present. The proximal segments of the limbs are particularly short. Of two cases in which the changes were apparently confined to one lower limb in one at the age of four weeks the affected limb was short while in the other though the legs were equal in length at sixteen months, there was one and a half inches of shortening at the age of nine years. Unfortunately full details are not available in either of these cases. The affected epiphyses are definitely enlarged. *Contractures*—Flexion of certain joints with a varying degree of limitation of movement was present in several cases the hips, knees, and elbows being the joints particularly affected. In one knee the head of the tibia was subluxated. The wrists were held in a flexed position in one case and there was ulnar deviation of both hands and rigidity of the wrists in another In yet another case there was contracture of the fingers. In two cases the hands were described as being long as compared with the forearm but in another the fingers were blunt and inclined to the accoucheur position. The feet in one case were rigid although the tarsal bones were not stippled In one case with involvement of a single leg the foot was valgoid and stiff. In two ases the limbs were said to be spastic but without further details while in a third the reflexes were much exaggerated. *Thickening of the skin* is mentioned by some German authors In Bateman s first case the skin of the palms was deeply furrowed and adherent to the deeper tissues particularly in the right hand which could not be opened completely The *head* has shown no characteristic features being variously described as normal rather large globular suggestive of oxycephaly bossed and even microcephalic. The fontanelle is large The nose in some was broad and the nostrils large. *Bilateral congenital*

Cataract has been a conspicuous feature of the British cases being found in six of the ten. Only in one of the cases reported in the literature of other countries is cataract mentioned *Intellect* appears to be distinctly dulled sometimes to the extent of mental deficiency *General weakness* failure to thrive and in one case cyanosis, were responsible for the patients being taken to hospital. *Blood examinations* have revealed nothing of interest

Radiographic appearances—In radiographs the *epiphyses* generally are stippled as if ossifying from many separate centres the appearance being suggestive of that produced by flicking paint from a brush on to a clean surface. The spots vary in size but most of them are minute and usually discrete. They also vary considerably in number and are not always more numerous in older than in younger children. There is evidence that in some cases the spots may become gradually smaller and fewer in number (Hünermann 1931 Hassler and Schallock 1940 and Jorup 1944) On the other hand they may show a tendency towards fusion with the formation of a single more normal centre of ossification. Often they appear at an earlier date than that at which ossification normally begins in the epiphysis concerned and they may appear too early by several years. For instance multiple centres were seen at the upper end of the ulna in a number of cases and in all these the olecranon epiphysis should not have been visible for some years. Abnormally early ossification stippled in character was also seen in the lower humeral epiphysis the radial head the floor of the acetabulum the ischial tuberosity and the neck of the scapula. Occasionally the carpus tarsus and patella also showed signs of premature ossification. Even though ossification in some epiphyses or in the carpus may proceed normally without stippling these centres may have appeared unusually early

The epiphyses most frequently showing the typical stippled appearance are those of the upper and lower ends of the femur upper end of the tibia, and upper end of the humerus. The lower end of the tibia both ends of the fibula the lower ends of the radius and ulna, and the bones of the hand are much less frequently affected. This affection differs strikingly from bone dysplasias generally in so far as characteristic changes are often shown in the region of the elbow joint multiple centres being found at the lower end of the humerus and in the radial head as well as in the olecranon. In at least four cases the femoral condyles showed a curious appearance the spots of ossification being arranged around the periphery in a curved line in two of these the outer condyle only was outlined in this way the inner showing just a few central spots. In a case with involvement of one lower limb there was at sixteen months an irregular mottled centre for the lower femoral epiphysis with in addition a separate group of small discrete centres for the medial condyle at nine years this epiphysis and that for the adjacent tibial head though both somewhat larger than the corresponding centres of the opposite leg were approximately normal in outline and density

In Lightwood s case (1930) more or less normal centres were present in the lower femoral epiphyses close to the metaphyses with additional stippled centres nearer the articular surfaces of the condyles. The stippling at the ends of the long bones is inclined to be erratic spots being sometimes seen where no part of an epiphysis should be found and perhaps absent where ossification should have begun It is often difficult to decide the correct allocation of the bony spots particularly if there is contracture of the knee or elbow joints and the shadow of the proximal bone is foreshortened.

In at least two patients the posterior ends of the ribs were stippled and this in spite of both being infants In the same two patients the thyroid cartilage showed signs of ossification and in one the hyoid was stippled Apart from stippling in the acetabulum and ischium already referred to the pelvis with one exception, was fairly normal in shape and appearance Stippling has not been seen in the iliac crests. In two patients aged four months and three weeks respectively the symphysis showed a dense median vertical line of calcification and in both wrists there was a single dense centre well to the inner side of the carpus. A similar curiously placed centre near the carpus was also seen in the first case reported by Bateman

(1936) but in this case two unstippled carpal bones were visible—the capitate and hamate. Stippling of the vertebrae was apparent in several cases and of the sacrum in four In at least two cases each vertebral body was ossifying by two separate centres, one in front of the other one of these (Lightwood 1930) was examined histologically by Professor H. A. Harris (1933) In a case published by Hassler and Schallock (1940) only a single centre was present for each vertebral body but stippling was seen in some of the intervertebral discs. These authors also reported calcification in the tracheal rings in the skin, and even in synovial membrane.

The shafts of the femora and humeri and occasionally of the tibiae are decidedly short and thick the ends being splayed to a marked degree with an irregular surface at the epiphysial line. At the upper ends of the femur and humerus the enlarged metaphysis often terminates in an oblique surface of considerable extent, being bevelled off on the inner side. In such cases it is difficult to visualise the cartilaginous epiphysis and to identify the anatomical site of the dense spots correctly At the upper end of the femur for instance the position of the spots sometimes suggests that the greater trochanter is ossifying before the head of the bone. The position of the femur in relation to the pelvis may suggest dislocation of the hip this being recorded in at least three cases (Lightwood 1930 Hassler and Schallock 1940) In several, the upper end of the ulna seems to be unduly prominent as if it were subluxated inwards in others, the lower end of this bone may be bevelled off on the outer side.

The condition of the tarsus varies ossification may be entirely by stippled centres, or the talus and calcaneus may be normal and only the heel apophysis show marked stippling long before ossification begins normally In two cases this apophysis appeared in a lateral radiograph as a vertical line, a considerable distance behind the calcaneus. In one case with changes confined to one leg, the front and back parts of the talus and the medial cuneiform, were stippled while the calcaneus, navicular cuboid and the greater part of the talus were of normal density Irregularity of the outline of the tarsal bones may be the only abnormality seen in the foot.

In one typical case at the age of three weeks (Hilliard 1943) the base of the skull was abnormally dense and the shafts of some of the long bones notably the tibiae and the metacarpals showed triangular dense areas towards each extremity while the talus and calcaneus, the only two tarsal bones ossified showed a circular line slightly more dense than the remainder of the bone, similar to that sometimes seen in osteopetrosis and in chronic poisoning by certain chemicals.

Progress—*At present it is impossible to say what the ultimate condition of the epiphyses may be* because no late reports of a case showing generalised changes are available. In the monomelic case already referred to which was re-examined at the age of nine years there was clear evidence of fusion of the discrete centres of ossification which had been present at an earlier age and of general improvement in the appearance of the epiphyses. However the ankle joint showed gross abnormality in the contour of the bones and a narrowed and irregular joint space suggestive of arthritis. The femoral head was enlarged and less convex than normal and the femoral neck was short and wide.

Early death—Half the patients are known to have died all but one before reaching the age of twelve months. The causes of death were infections involving the lungs or kidneys and miliary tuberculosis while in one case death occurred suddenly for no reason which was discovered.

Pathology—Harris (1933) reported patchy mucoid degeneration and cystic spaces in the cartilaginous epiphyses particularly near the articular surfaces. In some places the areas of degeneration were invaded by blood vessels and a core of fibrous tissue had formed. In the vertebral bodies which ossified from two centres there was failure of the usual orientation of cartilage cells and of normal calcification and ossification. Harris insists that the fundamental error is similar to that which he found in achondroplasia.

Hassler and Schallock (1940) made an exhaustive study of a child with this disorder who died a few days after birth. They found curious circumscribed polymorphous deposits of chalk in the cartilage and, near these, larger confluent areas of calcification. In other parts new bone formation was replacing the chalky areas. They also found diminution of the zone of ossification between bone and cartilage at the epiphyseal lines. In places this zone had disappeared completely.

Conradi (1914) illustrates star like foci of calcification in the cartilage. In the child reported by Lund (1942) who died at the age of four months the muscles were found to be replaced largely by tough fibrous tissue which apparently accounted for stiffness of the joints. In this case also histological changes in the bones were said to resemble those of achondroplasia.

Diagnosis—This must depend on radiographic examination. Discrete stippling as opposed to the mottling and epiphyseal irregularity seen in dysplasia epiphysialis multiplex and also sometimes in cretins is quite distinctive. If a case could be followed for a few years and the spots of ossification were given time to fuse the distinction would probably become more difficult. In a doubtful case the diagnosis is made easier if there is bilateral cataract.

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CASE 49—DYSPLASIA EPIPHYSIALIS PUNCTATA

(Fig 143) Child, aged one month with congenital shortening of the right leg The child died at age of nine months.



Fig. 143

Case 49—Right lower limb showing typical stippling of most of the epiphyses and of the tarsal bones Note that there are two separate groups of osseous centres for the femoral condyles. The tibial head is subluxated

CASE 50—DYSPLASIA EPIPHYSIALIS PUNCTATA

(Figs. 144 to 147.) Female child aged two and a half years. Parents normal. Failed to develop normally from birth. Mentally dull. Double congenital cataract. Marked bossing of skull. Fontanelle closed. Enlargement of epiphyses. Beading of ribs. Fingers have blunt square extremities. Limitation of movement of knees and elbows. Wassermann negative. Thyroid administration gave no improvement. Gradually wasted and died of pneumonia when aged three and a half years. (Under Dr Eric Pritchard.)



FIG. 144

Case 50—Right leg showing typical appearances: femoral shaft short, thick, and strong, with metaphyses splayed and the epiphyses stippled. Note the stippling in the ischial tuberosity as well as in the acetabular cup.



FIG. 145

Case 50—Pelvis and hips showing curious shape of the ilia, and, on each side, stippling of the acetabulum and upper extremity of the femur.

CASE 51—DYSPLASIA EPIPHYSIALIS PUNCTATA

(Figs. 148 to 150) Girl aged four months Very feeble Large head distended veins fontanelles widely open nose depressed Limbs short particularly the proximal segments Hips knees and elbows flexed and cannot be extended fully Feet solid Ulnar deviation of hands Wrists stiff Reflexes accentuated Blood chemistry normal Bilateral congenital cataract Died during a feed for no discoverable reason (Under Dr W G Wyllie Case reported by Dr E. Lund, 191* under another title)



FIG. 148

Case 51—Pelvis and femora, showing central linear ossification in the symphysis premature stippled ossification of the ischial tuberosities and of the acetabular floor short thick femora (partly due to fore-shortening) and general stippling of the shapeless upper end

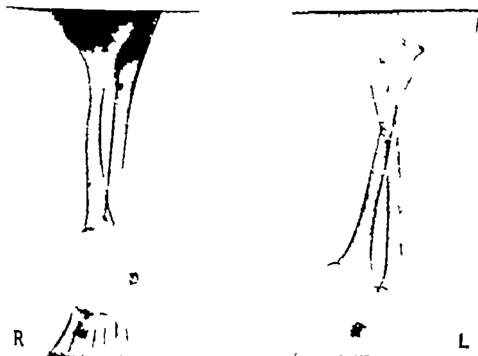


FIG 149 FIG 150

Case 51—Forearms showing the curious dense ossified spot at the inner side of each wrist joint Stippling in the region of the elbow including premature ossification in the radial head can just be seen.

CASE 52—DYSPLASIA EPIPHYSIALIS PUNCTATA

(Figs. 151 and 152.) Male child, aged eleven months—only child of normal parents. Limbs short particularly the proximal segments. Limitation of movement of hips. Double congenital cataract. Died within a few weeks of acute miliary tuberculosis. (Under Dr R. C. Lightwood who published the case in 1930.)

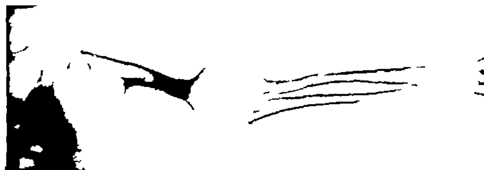


Fig. 151

Case 52—Left upper limb showing short, thick humeri with splayed metaphyses and bevelling on the inner side of the upper metaphyses, and subluxation inwards of the ulna at the elbow. In addition to stippling at the shoulder and elbow.



Fig. 152

Case 52—Pelvis and femora showing typically short thick femora with bevelled upper extremities and stippling of epiphyses at both ends. Note the apparent dislocation of the hip joints and the premature ossification of the greater trochanters. The lower femoral epiphyses show centres close to the metaphyses, in addition to stippling confined to the outer condyles.

CHAPTER 10

OSTEOPATHIA STRIATA

This very unusual affection is characterised by striation of the skeleton and particularly of the metaphyses of long bones In 1924 Voorhoeve published three case reports a father and two children in which radiographs showed striation of the metaphyses with other minor changes in the bones which had not been described before Shortly afterwards the author published a report of the clinical findings in a boy aged twelve years with predominantly unilateral changes in which striation was a prominent feature (Fairbank 1925) and Dr Voorhoeve agreed that the case was similar to those he had described. Striation of the bones was also a striking feature in an unpublished case brought to my notice by Dr Grace Batten but it differed in many respects from those mentioned above and will be considered separately with a similar case published by Uehlinger (1941)

In 1935 the author suggested osteopathia striata as a title for this obscure condition Two rather similar cases a brother and sister were published by Lindbom (1942) under the title of striated osteopoikilosis (Voorhoeve) but they are exceptional in many ways, being neither quite like Voorhoeve's cases nor like osteopoikilosis. Lindbom believed that disseminated dermato-fibrosis in his two cases reinforced the concept that the striation was related to osteopoikilosis.

Hereditary and familial influences were evident only in Voorhoeve's original three cases. *Sex*—Three of the four cases were males. *Age*—Three of the cases were young their ages being ten, twelve and fourteen years respectively the fourth was the father of two of these children. *Etiology*—The cause is unknown the author considers that it is the result of a congenital developmental error Voorhoeve suggested that the striated bones he had described were related to dyschondroplasia and osteopoikilosis the three disorders being variants of the same fundamental error with the first forming a link between the other two but this writer hesitates to accept such a view particularly with regard to osteopoikilosis.

Clinical features—There appear to be no symptoms definitely referable to the bone dysplasia. Vague recurrent joint pains with or without a little swelling were complained of in the hip and knee joints of one patient and in the shoulder joint of another The author's patient had suffered rheumatic fever affecting his heart and in this unilateral case an abnormal gait and "awkwardness" had attracted the attention of the parents to the affected limb for some years and for this reason radiographic examination was made The limb was longer and thinner than on the opposite side, but the upper limbs were of equal length. Otherwise there were no abnormal physical signs. *Blood examination*—Nothing of importance was discovered.

Radiological examination—The outstanding feature is striation affecting in varying degree all bones with the exception of the skull and clavicles. In the long bones the striation affects principally the metaphyses the dense lines run parallel to the long axis of the bones and can be traced for a considerable distance into the shafts. The thickness of the striations varies but most of them are fine and linear Between the lines the bones may be porotic. Voorhoeve called attention to the appearance of both clear areas and dense spots in certain bones and he pointed out that in some places one of the dense lines appeared to break through the cortex. The striation may or may not extend into the adjacent epiphysis. Sometimes the epiphyses are mottled with dense and clear spots. The clavicles are not affected. The hands are less affected than the rest of the skeleton. Striation is well seen in the tarsus and especially the calcaneus. The patella may be affected. In at least one of Voorhoeve's cases the boy of fourteen years the ilia were striated with lines radiating towards the crests like

the columns of cartilage in dyschondroplasia. In our unilateral case there was a dense patch in the ischium on the side on which the striation of the long bones was more obvious and a few irregular dense spots in the opposite ischium these features being even more marked in radiographs taken some years later Usually the cortex of the bone is of normal thickness and density and there is no distortion. Voorhoeve however called attention to the presence of exostoses in his cases these were very small and were not found in the other case

Pathology—So far no pathological material has been available for investigation but it *seems probable that microscopic examination would reveal only normal bone of varying* density Striation of the metaphyses, in our case at any rate does not appear to have been the result of any epiphysial fault Early radiographs of the lower femoral and upper tibial metaphyses showed that the most recently formed bone to a depth of half an inch, was less dense than that formed earlier and that these clear bands were largely free from the dense striation visible in the adjacent parts of the shafts whereas radiographs taken four years later showed no clear bands in these bones, and the striations extended through the metaphyses to the epiphysial lines. Thus the dense lines had developed *after* the bone forming the clear bands had been ossified. The region of the knee joint was the only place where juxta-epiphysial clear bands were visible in the early films.

Diagnosis—In dyschondroplasia the bone between the columns of unossified cartilage often gives rise to a striated appearance but this is never seen with such regularity in every major metaphyses as in osteopathia striata. Moreover in osteopathia striata the long bones of the hand and foot are less affected than the major long bones whereas in dyschondroplasia the hands, and to a lesser extent the feet are the chief seats of changes which could never be described as striation Reference has already been made to the fan like arrangement of striation which may be seen in the ilia in both these disorders.

The few dense spots seen in these cases are a little suggestive of those seen in osteopoikilosis but in typical cases of osteopoikilosis certain parts of the skeleton, particularly the epiphyses are closely peppered with dense spots. It is true that the spots in osteopoikilosis may be prolonged in some places into streaks but these are much shorter and much less regular than the dense lines seen in osteopathia striata.

Striation may be seen occasionally in one or two long bones in several other conditions but it is never distributed widely throughout the skeleton as in this affection In melorheostosis dense streaking may be seen, but only to a very limited extent and only in one or two bones, while the character and limited distribution of the other changes are usually typical. In diffuse fibrosis of bone (polyostotic fibrous dysplasia) patches of increased density ending in two or three broad streaks may be seen in the radiographs but only in one or two bones.

The later films of the knee joint on the more affected side in our case showed some enlargement of the femoral and tibial shafts (enlargement of the fibula was noted in the earlier films) and the radiographic picture had become a little suggestive of that seen in diffuse fibrosis The possibility that the affection in our case may not be identical with that responsible for Voorhoeve's cases cannot be entirely discarded Similar increase of density ending in streaks may be seen in one or two long bones in neurofibromatosis but this should be recognised without difficulty by other features. We have seen striation in the region of the knee joint in an atypical case of osteopetrosis. In Paget's disease an appearance worthy of the name of striation is exceptional but it may be quite marked in the os calcis at early stages of the disease

GENERALISED HYPEROSTOSIS WITH PACHYDERMIA

In 1941 Uehlinger published the report of a case of hyperostosis generalisata mit pachydermie affecting chiefly the long bones with coarse striation of a considerable part of the skeleton Dr Grace Batten's case referred to above appears to be identical except that there was no pachydermia. Uehlinger referred to a number of other cases some published

before the discovery of X rays which he believed to be similar to the one he described. A familial tendency was apparent in many of them and skin changes affecting particularly the distal segments of the limbs were present in some but not all. Other writers have linked these cases with pulmonary hypertrophic osteoarthropathy—for example Freund (1938) despite the absence of changes in the chest and the marked differences in the radiographic appearances—but Uehlinger did not accept this view Among the cases published with radiographs we have failed to find a single case that was strictly comparable with the patient reported by Uehlinger in none was striation an outstanding feature Uehlinger's patient was a farm worker who died at the age of fifty five years the condition of the bones having been discovered incidentally at the age of forty-one years when a radiograph had been taken during the treatment of an infected toe Difficulty in walking over rough ground, and undue fatigue had been noticed for about one year There was disproportionate length of the lower limbs and both forearms and legs were noticeably stout the skin being thick and leathery The spine was very stiff chest expansion was limited and there was limitation of movement of several other joints. Later the patient complained of constant pain in the bones and in the abdomen together with difficulty in micturition which was attributed to spinal compression. The contracture of the limbs increased and he became bedridden. There was bilateral cataract and clubbing of the fingers but no calcification in the kidneys or arteries. Little advance in the bone changes occurred during the last ten years of his life After death, examination of the bones showed that the marrow was fatty and not fibrotic the hyperostotic bone was mostly of the woven type Dr Batten's case also a male was above the average in height his legs showed no obvious thickening and there was no pachydermia

The cause of the condition seen in these two cases is unknown. In the second case there was a history of long-standing semi-starvation and the physicians considered that he had probably suffered from protein deficiency over a period of years.

The radiographic changes in these cases are of two kinds 1) coarse striation of cancellous bone and 2) thickening of the cortices of long bones. The striation is much coarser than that seen in osteopathia striata, and it is seen particularly well in the metaphyses and epiphyses of the long bones the vertebrae and the tarsus. The hyperostosis, which on the whole is more pronounced on the external than the internal surfaces of the cortices, is seen on the shafts of all long bones. The density of the new bone varies considerably In the metacarpals metatarsals and to a lesser extent the phalanges there is no more than increased thickness of the dense cortices. In the major long bones the new bone is more variable in density though on the whole it is less dense than normal cortical bone and shows an irregular fluffy surface Some of these thickened bones are irregularly honeycombed, the appearance being rather suggestive of Paget's disease The hyperostosis of the long bones was more advanced and more universal in the patient reported by Uehlinger possibly because he was twice the age of Dr Batten's patient The skull ribs and vertebral bodies were comparatively free from cortical changes. In Uehlinger's case there was fusion of the lateral articulations and ossification of the dorsal ligaments throughout most of the spine the vertebral bodies showed well-marked vertical striation in both cases. The pituitary fossa appeared to be normal.

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CASE 53—OSTEOPATHIA STRIATA

(Figs. 153 to 157) Male first seen when twelve years of age Always ran awkwardly something wrong with right leg At ten years developed rheumatic fever which affected his heart no definite arthritis at any time Awkwardness of right leg more noticeable recently Family history negative. On examination—no limp Right thigh thinner than left calves equal *right lower limb half an inch longer than left Movement of all joints free.* Heart loud mitral murmur Urine contained trace of albumin no Bence-Jones albumose Radiographs showed striation affecting particularly the right side of the pelvis the right half of the sacrum, and the bones of the right lower limb The bones of the right upper limb including the glenoid and acromion were also affected but not to the extent seen in the lower limb The bones of the right side were generally more translucent than those on the left and this accentuated the striated appearance. There was a little mottling with dense spots in some of the epiphyses and in the cuboid. The shaft of the right fibula was thickened. The bones of the left upper and lower limbs were not entirely free from changes but these were much less marked than on the right side. There was one dense spot in the right capitate and some mottling of the right ischium. The skull showed nothing abnormal. Radiographs taken four years later showed even more marked striation the bones on the right side still showing more advanced changes than on the left. Osteoporosis in the bones of the right side had practically disappeared. The right ischium showed an area of increased density there were a few dense spots in the left ischium. At the age of twenty years there were no symptoms referable to the bone dysplasia.



FIG 153

Case 53—Pelvis and hip joints at the age of twelve years, showing on the right side some osteoporosis and dense striation with mottling in the head of the femur the ilium and the tuber ischii. On the left side the only abnormal feature is slight striation of the femur

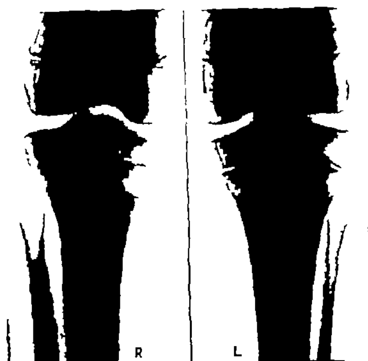


FIG. 154

Case 53—Knee joints at the age of twelve years. Striation of the shafts and epiphyses is more marked on the right side. Right fibula is thickened.

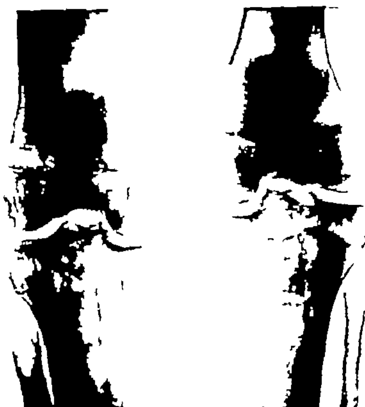


FIG. 155

Case 53—Knee joints at the age of sixteen years. There is striation of both femora and tibiae. The shaft of the right tibia is now slightly enlarged as well as the fibula.

Fig. 156

Case 53—Pelvis and femora at sixteen years, showing striation, more marked on the right side, and dense spots in the head of the right femur, the right ilium and in the left ischium. In the right ischium is a dense patch. Note that the osteoporosis on the right side is now much less obvious.

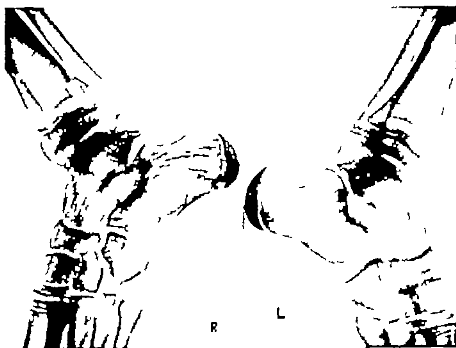


Fig. 157

Case 53—Ankles and feet at sixteen years. Striation is more obvious on the right, partly owing to the diminished density of the bones.

CASE 54—OSTEOPATHIA STRIATA

(Figs. 158 and 159.) Boy aged fourteen years. For three years he had complained of recurrent attacks of pain and swelling of the left knee joint; the attacks lasted from a few days to a week and then cleared up completely. At four years had scarlatina followed by rheumatism; recovery was complete. The blood and urine were normal. Radiographs showed marked striation of the metaphyses of all the long bones, the sacral wings, pelvis, patellae, calcanei, scapulae and the ribs near the costo-chondral junctions. There were also some clear areas and dense spots in the bones with slight enlargement of the metaphyses and a few small exostoses. His father to a small extent and his sister showed similar changes. (Dr Voorhoeve's case.)



Fig. 158

Case 54—Knee joint showing marked striation with slight enlargement of the metaphyses, and a local projection resembling an exostosis on the inner side of both femur and tibia (after Voorhoeve.)



Fig. 159

Case 54—Pelvis and upper femora showing striation which radiates in the iliac bones. The necks of the femora are rather thick and both show a tiny spur projecting downward. (After Voorhoeve.)

CASE 55—HYPEROSTOSIS GENERALISATA with striation of the bones

(Figs. 160 to 166.) Male aged twenty-eight years. Admitted to hospital with pneumonia. Had always been healthy but underfed. Investigations into his history showed that there had been prolonged deficiency in calcium, and vitamins A, B_1, C and D. Probably a protein deficiency over a period of many years. Repeatedly unemployed. His father and an uncle said to be of same build as himself. Other members of family normal. Patient is well above the average in height and is thin. Blood examination—negative. Radiographs showed coarse striation of the ends of most of the long bones and of the vertebral bodies, tarsus, sacrum and less obviously the pelvis and ribs. The hands and feet show increased thickness, with uniform density of the cortices of the minor long bones. There is a varying degree of hyperostosis of the major long bones, and the normal contrast between cortex and medulla is obscured. On the whole the surface of the thickened bones is fairly smooth. The left tibia shows fusiform enlargement posteriorly in the upper half due to thickening of the cortex. Except for slight increase in density the skull shows no definite change. (By courtesy of Dr G. Batten.)



FIG. 160



FIG. 161

Case 55—Note the lanky build of the patient (Fig. 160). Radiograph of the spine shows coarse vertical striation of the vertebral bodies (Fig. 161).

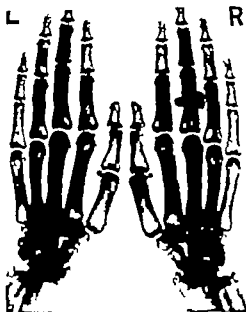


Fig. 162

Fig. 163

Case 55—Radiographs of the hands and foot show thickening of the cortex of the metacarpals and metatarsals (Figs. 162, 163) striation of the tarsal bones and the ends of all the long bones. The density of the carpal bones is irregular.



Fig. 164



Fig. 165



Fig. 166

Case 55—The humerus shows altered texture and increase of density but no enlargement of shaft (Fig. 164). The forearm shows hyperostosis (Fig. 165). In the knee joint there is coarse striation and enlargement of metaphyses (Fig. 166).

CHAPTER 11

OSTEOPOIKILOSIS

Synonym—Osteopathia Condensans Disseminata

This is an unusual affection of the skeleton characterised by multiple dense spots in many bones. It was first described by Stieda (1905) but is usually ascribed to Albers-Schönberg who published a more typical case in 1915 The title now commonly used is derived from the word l osteopoécilie suggested by Ledoux Lebard et al in 1916 The longer alternative name—osteopathia condensans disseminata—we owe to Wachtel (19*1)

Hereditary and familial influences are frequently in evidence It has been observed in three generations (Busch 1937 Hinson 1939)

Sex—Males are affected more than twice as commonly as females

Age—It has been found at all ages from foetal life to over sixty years. By some it is thought always to be congenital. Most of the spots however are seen in parts of the bones which are certainly not ossified until after birth.

The cause is entirely unknown. The affection gives rise to no symptoms and it is always discovered by chance.

Blood examination reveals nothing of importance.

Radiographic appearances and distribution—The dense spots are circular ovoid or lanceolate the long axis of each being parallel to the long axis of the affected bone They vary in size between two and ten millimetres. As a rule they are of uniform density but they may have relatively clear centres. They occur particularly in the epiphyses and adjacent parts of the metaphyses and are plentiful in the short bones of the carpus and tarsus. They vary in number in most cases they are numerous and are found in every bone with the exception of the skull, ribs, and vertebrae. Even in these bones one or two spots have been seen the skull being the most unusual site of all The pituitary fossa is often small and largely covered in by the posterior clinoid processes. The lower jaw is an unusual site for a spot When present in the spine they are usually in the accessory processes but they have been observed in a vertebral body In the pelvis they are common and numerous. In the ilium they are usually congregated near the acetabulum the sacro-iliac joint, and the crest leaving the central part of the bone clear

The spots are in cancellous bone and as a rule they are entirely free from the cortex which is never distorted in any way Sometimes a spot of dense bone is prolonged into a short streak in the axis of the bone especially when it is situated some distance from an epiphysial line where the metaphysis of a major long bone is passing into the shaft. In the shaft itself spots are seldom seen. These streaks are much shorter more irregular and more fluffy in outline than the larger strands of dense bone which are seen in melorheostosis and in some cases of diffuse fibrosis of bone When the spots are numerous and crowded together as for example in an epiphysis the relatively large and irregular dense area thus formed gives the impression of a conglomeration of spots the apparent fusion is probably due more to overlap of shadows than to actual coalescence

In the clavicle spots are uncommon the outer extremity being the most frequent site In the scapula the acromion is the usual site. In the metacarpals, metatarsals and phalanges spots may often be seen in the centre of the shafts as well as in the epiphyses.

Progress—Cases have been observed over a number of years with no apparent change in the radiographic appearances. In general this seems to be true of patients in whom growth has ceased. Holly (1936) however claims to have seen spots fuse others disappear and new

spots develop especially in children New spots must appear during growth of a bone to give the appearance seen in adult life.

Complications—Several cases have been reported in which the condition has been associated with dermatofibrosis lenticularis disseminata. (Buschke and Ollendorff 1928 Windholz 1932 1933 Svab 1932 Busch 1937 Lindbom 1942)

Pathology—On microscopic examination the spots are found to consist of numerous regularly arranged trabeculae of varying thickness some being thicker than normal and lying for the most part in the axis of the bone The general appearance suggests dense spongiosa rather than cortical bone (Schmorl 1931) At the periphery they merge into surrounding cancellous bone There is nothing to suggest that the spots are endochondral in origin and they have no connection with epiphysial cartilage. Occasionally a trabecula is formed around a blood vessel There is no sign of fibrosis of the marrow (Schmorl 1931)

Diagnosis—In melorheostosis similar spots in the epiphyses carpus and tarsus form a minor feature but they are more irregular in shape and size and are better described as blotches or splashes than conglomerations of spots. The dense flow or broad bands of dense bone in the shafts of long bones determines the diagnosis. In melorheostosis the greater part of a short bone may be occupied by a single patch of dense bone while in this condition dense spots may be seen in the soft tissues a condition never found in osteopoikilosis Cases have been published under one or other of the two titles at the head of this chapter which we would prefer to classify as melorheostosis and vice versa. In one case (Nichols and Shiflett 1934) the two conditions really did seem to be associated

Dense spots occur in the cartilage masses of metaphyses in dyschondroplasia, usually when growth is approaching completion in adolescence Otherwise, radiographs in the two conditions have little in common For instance in osteopoikilosis the epiphyses are peppered with spots whereas in dyschondroplasia, though an epiphysis may be mottled this is never seen without change in the adjacent metaphysis which makes the diagnosis clear I can see no sufficient reason for regarding the changes characteristic of these two affections, and the marked striation seen in the case published by Voorhoeve (1924) as fundamentally the same although this was suggested by that author In 1942 Lindbom reported two cases under the title of striated osteopoikilosis (Voorhoeve) These cases a brother and sister are exceptional in many ways and are neither quite like Voorhoeve s case nor like osteopoikilosis He believed that the disseminated dermatofibrosis which was present in these two children strengthened the concept that the striation is related to osteopoikilosis.

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CASE 56—OSTEOPOIKILOSIS

(Figs. 167 to 170.) Male aged twenty-one years. Condition of the bones found by chance, when an injury of the knee joint was investigated. It is a well-marked case with numerous spots in most bones. (Under Maj.-Gen. J. W. West.)



Fig. 167

Case 56. Wrists and hands showing typical dense spots, thickly distributed in the lower epiphyses of the radii and ulna, and in the carpal bones. Note that the spots are seen also at both ends of the metacarpals and not only in the old epiphyses.



Fig. 168

Case 56. Pelvis and upper femora showing spots distributed freely in all bones including the sacrum. Note that the greater part of both ilia is free from spots.

Fig. 169



Fig. 170

Case 56—Knee and foot showing typical spots widely distributed. Note a few spots in the femoral and tibial shafts

CHAPTER 12

CHONDRO OSTEO DYSTROPHY

Morquio-Brailsford Type

This disorder is characterised by dwarfism with shallowness of the vertebral bodies marked kyphosis, sometimes angular increase of the spinal curve at the dorso-lumbar junction and progressive changes in the femoral head and acetabulum in a child of normal intelligence It lacks the special features that are characteristic of the other type of chondro-osteo-dystrophy known as gargoylism. To a varying extent the whole skeleton is affected, with the exception of the bones of the skull and face which are usually normal

The condition is generally associated with the names of Morquio and Brailsford. Cases that we should now place in this group were undoubtedly published under various titles before 1929 but in that year Morquio described A Form of Familial Osseous Dystrophy" seen in four members of a family of five and Brailsford suggested chondro-osteo-dystrophy as a suitable title for the condition he found in one patient the radiographic changes of which were described in detail. In 1930 Wheeldon reported two patients with achondroplasia but with the unusual feature of a wedge-shaped vertebra which is so often a characteristic feature of both types of chondro-osteo-dystrophy and one of these patients was later followed up and reported by Pohl (1939) as an example of Morquio s disease. In 1925 at the Royal Society of Medicine, Thursfield showed A Case of General Enlargement of Joints" which this author had seen with him, and which he published with illustrations in 1927 this case we should now place in the group under discussion. Many others have since been reported.

Hereditary and familial influences—Hereditary influences are seldom apparent, whereas familial influences are common. Statistics vary because of differences of opinion whether or not individual cases should be included. Of the sixty cases known to this author which he believes should be classified in the group it was found that another member of the family was affected in about one-third. Jacobsen (1939) reported twenty members in five generations of one family affected by a condition which, though not typical, appears to be allied closely with the Morquio-Brailsford syndrome

Sex—Both sexes are affected, males slightly more often than females.

Age—Some abnormality may be present at birth (Hirsch 1937) but the developmental error is seldom apparent until the child begins to walk and appreciable changes are often first recognised at about the age of 4 years or even later Only six patients in the series studied by this author were seen under the age of 4 years but thirty-six (60 per cent.) were under 10 years of age.

Etiology—The possible causes have been discussed by many authors but without any convincing evidence and it must be acknowledged that the cause is unknown. Ashby Stewart and Watkin (1937) suggested that the disorder will eventually be included with gargoylism in the group of lipoidoses.

Clinical characteristics—At about the age of 4 years it may be noted that there is curvature of the spine failure to gain normal height, and the development of symmetrical deformities which increase with progressive crippling until the child is unable to walk without aid. The typical appearances are those of a round-backed, knock-kneed, flat footed child who stands with the hips and knees flexed in a crouching position with the head thrust forward and sunk between high shoulders looking not unlike a case of cervical caries, and walking in the waddling manner of a duck (Morquio 1929) The face is intelligent but perhaps inclined to conform to an almost characteristic type. The bridge of the nose may be depressed and the eyes widely separated the head may be large but it is usually normal in size and

shape the neck is short There is marked kyphosis of the spine with a short lordotic curve below In about one-third of the patients there is angular accentuation of the kyphosis in the dorso-lumbar region which may suggest caries of the spine but pain in the back is most unusual. There is always limitation of movement particularly of extension of the spine and there may be scoliosis. The chest is narrow and the antero-posterior measurement is increased, the sternum being thrust forwards (pectus carinatum) Muscle weakness without changes in the electrical reactions has been noted. The spleen and liver may be felt rather easily but they are not enlarged

Though the child is dwarfed generally it is shortness of the spine that is chiefly responsible for the lack of height. The limbs are relatively long It has often been recorded that in the standing position the hands reach almost to the level of the knees. Dwarfing of the proximal segments of the upper limbs, which is so marked a feature of achondroplasia was noted in only one of the sixty cases. Some authors have said that there is congenital elevation of the scapula (Sprengel's shoulder) but their description of the mobility of the scapulae hardly agrees with the usual finding in this deformity

The epiphyses are often but not always enlarged. In some joints there is limitation of movement whereas others show hypermobility this variable feature being evident sometimes in different joints of the same patient As would be expected from the radiographic appearances there is often stiffness of the hip joints and less frequently of the shoulders knees ankles elbows, wrists, fingers and toes. General stiffness involving many joints was a feature in seven patients. Laxity of ligaments with hypermobility is seen most often in the wrists fingers feet and toes and less often in the knees and ankles. It may be possible to dorsiflex the wrists until the fingers touch the back of the forearm. In one unpublished case of a boy aged 4 years with widespread laxity of ligaments several joints could easily be dislocated and both patellae dislocated whenever the knee joints were flexed Knock-knee and other deformities occur at the joint level or close to it and are not the result of bending of the shafts of the bones they tend to become gradually worse

The fingers are usually broad and blunt Enlargement of the interphalangeal joints of the fingers was a striking feature in four patients, and to a less extent in a fifth, the swelling suggesting polyarthritis but the enlargement was due to thickening of the bones and not to swelling of the joints. Widespread stiffness involving many joints was a feature of these cases (Thursfield 1925 Scott 1929 Ellman 1932 Hardwick 1938)

Pain is unusual but as bone changes in the hip joints increase there is sometimes pain in this region which may be the first symptom responsible for the child being taken to hospital. *Blood examination* reveals nothing of importance The serum calcium may be raised lowered or normal

Radiographic appearances—General porosis of the skeleton has often been noted This is of no diagnostic importance and it is almost certainly no more than the result of limited activity due to crippling The spine shows flattening of the vertebral bodies which may be more obvious in the dorsal than in the lumbar region There is platyspondyly with increase in the transverse diameters and particularly in the antero-posterior diameters of the bodies. In lateral radiographs the bodies have a characteristic shape by which they can be distinguished readily from the typical vertebral bodies of gargoylism. The upper and lower surfaces are irregular ill-defined and defective with a tendency to approximate towards each other in front thus accounting for a wedge-shaped appearance which is accentuated by a central prolongation or tongue Later on, multiple centres appear by which the defects are repaired and the epiphysial rings formed (Brailsford 1944) In the lumbar bodies a layer of less dense bone has been seen above and below with a more dense layer between (C[illegible]rin and Lachapele 1938) The typical shape is most obvious in the lower dorsal and upper lumbar regions the lower lumbar vertebrae tending to be more normal in shape When there is an angular kink in the spine lateral radiographs show that one vertebral body

at the dorso-lumbar junction is smaller than the others and is displaced a little backwards as if it had been squeezed out of position by the bodies above and below This mal-alignment is always more obvious immediately above the small body than below it in fact the appearance suggests that the spine above has slipped forwards on the small wedge-shaped body The first lumbar vertebra is most often affected in this way but the anomaly may be seen in the twelfth dorsal, and occasionally in the eleventh dorsal vertebra. The second lumbar vertebra was the centre of a kink in one patient and the third lumbar vertebra in another The body next below the displaced one was also rather small in three cases (Summerfeldt and Brown 1936 Pohl 1930) the body next above was reduced in size in only a single unpublished case. As a rule the intervertebral discs are relatively deep but occasionally they are reduced in depth. The pelvis may be narrow or shaped as in the ape. The ribs are more horizontal than usual and they are expanded at both extremities.

There is usually irregularity in outline of at least some epiphyses. The hips are always affected, the changes becoming progressively more marked as the child grows. The acetabula are enlarged and irregular The femoral heads are irregular flattened and fragmented. Sooner or later the femoral necks appear short thick and spread, with coxa vara. Examination of radiographs taken at intervals of three to six years in four cases in the author s collection shows not only that changes are definitely progressive but that the femoral heads may be normal to begin with and only later show signs of faulty development or degeneration. There may be incomplete or complete dislocation of the hip joints on one or both sides. In one patient there was no displacement of the femora at the age of 9 years and yet both hip joints were dislocated when re-examined at the age of 15 years. Other epiphyses that sometimes show degenerative changes are those at the lower end of the femur upper end of the tibia (Ruggles 1931) and upper end of the humerus but it is only the changes in the hip joints that are important from the diagnostic point of view Several or many epiphyses were said to have been affected in seven cases. It is also said that irregularity and fragmentation of the epiphyses may disappear later Delay or irregularity in ossification may be seen in the patella.

The joint spaces appear to be unusually wide in younger children The shafts of the major long bones are usually normal but occasionally they are short and thick. There was symmetrical thickening of the cortex on the outer side of the upper femoral shafts in one patient—a curious feature that has been seen in only two other patients both suffering from gargoylism The metaphyses may be splayed to accommodate the enlarged epiphyses especially in the radius and ulna where the epiphysial lines at the lower ends are tilted towards each other The ulna, as in so many developmental errors, may be short The fibula may also be short whereas in achondroplasia it is usually long

The metacarpals and phalanges are stubby with expanded ends. The bases of some metacarpals especially the third and fourth, and the distal extremities of the phalanges, tend to be pointed. There may be multiple centres of ossification for the epiphyses of the hands and feet Ossification of the carpus may be delayed and when the bones are ossified they may be irregular in outline. There may also be irregularity in shape of the tarsal bones. In one case included with confidence in this group because of other skeletal changes the great toes were abnormally long and large the first metatarsals sharing enlargement with the phalanges (Thursfield 1925)

Changes in the skull are usually minimal and unimportant. The pituitary fossa is usually normal it has sometimes been found small and sometimes enlarged. Digital markings in the skull were seen in two brothers in a family of eight children in which a third member showed signs of the Morquio-Brailsford affection.

Progress—As a rule radiographic changes in the bones advance and deformities progress with increasing disability until walking becomes impossible without assistance.

Pathology—The pathology is unknown. Shelling (1945) examined biopsy specimens from the lower femoral epiphysis and diaphysis in one case the epiphysial line was irregular

there were cartilaginous nests within the bony trabeculae and the matrix in these nests was striated and stained in an irregular manner Harris and Russell (1933) believed that mucoid degeneration of cartilage in place of normal calcification was the fundamental change in dwarfism including achondroplasia.

Differential diagnosis—Many examples of Morquio-Brailsford chondro-osteo-dystrophy have been reported as cases of achondroplasia, with or without the prefix atypical but as a rule the appearances of the head and face in chondro-osteo-dystrophy are quite unlike those of achondroplasia In achondroplasia there is apparent lordosis with prominence of the buttocks less secondary kyphosis normal length of the spine shortening of the limbs and particularly of the proximal segments and usually bowing of the legs rather than genu valgum.* There is seldom coxa vara in achondroplasia and there are never the gross epiphysial and articular changes seen in the Morquio-Brailsford affection. The achondroplasiac patient is sturdy and strong he is not feeble as are the patients discussed in this chapter

The special features of gargoylism, the other type of chondro-osteo-dystrophy are the heavy facies mental deficiency cloudy corneae and enlargement of the liver and spleen. In gargoylism the spine may also show a kink in the dorso-lumbar region with one vertebral body small and displaced backwards, but the shape of the bodies differs markedly from that seen in the Morquio-Brailsford type Very seldom is there difficulty in deciding to which group a case belongs after examination of radiographs of the spine but the one described by Snoke (1933) is an exception

When many epiphyses are involved the condition must be distinguished from dysplasia epiphysialis multiplex in which the spine is usually normal and the acetabulum is not altered in the way that it almost invariably is in the Morquio-Brailsford syndrome Only two examples of multiple epiphysial dysplasia with flattening of the vertebral bodies are known to the author When the patient complains only of the hip joints local radiographic changes might suggest the diagnosis of pseudo-coxalgia were it not for the striking deformities of the trunk.

Deformity in the dorso-lumbar region du to wedging of a vertebral body may be seen occasionally in cretins, and also in normal foetal life (Report of the Institute of Social Medicine Oxford 1946) The appearances in one patient seen by the author would suggest that the abnormality in shape of the vertebral bodies in cretins is of the type seen in gargoylism rather than that of this type of chondro-osteo-dystrophy A similar local deformity of the spine has been seen in a child who appeared to be entirely free from other skeletal abnormalities.

The di tinction from spinal caries of the dorso-lumbar region should be made without difficulty after examination of lateral radiographs of the spine It must be recognised, however that a degree of dwarfism is a feature of several conditions, and atypical cases occur which for the moment it is difficult to classify with any degree of conviction.

* It is true that in two nquestionable cases of achondroplasia there was an angular kyphosis at the dorso-lumbar junction In one of these a ertebral body t the angle was smaller than the others. But in neither were the ertebrae flattened and spread

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CASE 57—CHONDRO-OSTEO-DYSTROPHY (Morquio-Brailsford Type)

(Figs. 171 to 175) Boy aged four and a half years. Enlargement of joints and other deformities first noticed after an attack of bronchitis when six months old. Did not walk until the age of three and a half years. Family history negative. Clinical features—kypho-scoliosis with



FIG. 171

Case 57—Photographs of the child aged four and a half years, showing thickening of the ends of the bones and lengthening of the great toes. Note the kyphotic curve, and the typical standing attitude with the hips and knees flexed.

enormous enlargement of the epiphyses and lengthening of the great toes (an exceptional feature) some limitation of rotation movement at the shoulder joints and of pronation and supination of the forearm Fingers thick and stumpy nails unusually short unable to flex the fingers properly especially at the metacarpo-phalangeal joints Backward child. Head rather large (Under the late Dr Hugh Thursfield. Reported Thursfield 1925 Fairbank 1927)



Fig. 17?

Case 57—Upper limb, showing the short bones with enlarged ends and some irregularity of ossification of the epiphyses.



Fig. 173

Case 57—Lateral radiograph showing increased antero-posterior measurement of the bodies, disc spaces not unduly wide, no abrupt kyphos at the dorso-lumbar junction.

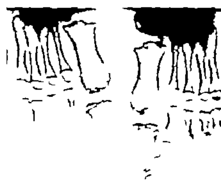


Fig. 1 4

Case 57—Enlargement of the great toes with irregular ossification at both ends of the first metatarsal and the proximal phalanges.

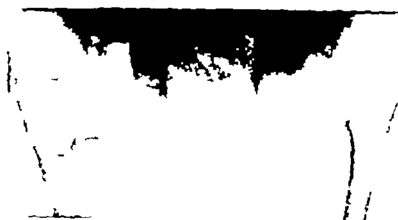


Fig. 1 5

Case 5 [illegible] showing ape-like shape of the pelvis, poorly developed acetabula and marked coxa vara with delayed and irregular ossification of the femoral heads.

MORQUIO, L. (1929) Archives de Médecine des Enfants, 32, 129
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CASE 37—CHONDRO-OSTEO-DYSTROPHY (Morquio-Brailsford Type)

(Figs. 171 to 175) Boy aged four and a half years. Enlargement of joints and other deformities first noticed after an attack of bronchitis when six months old. Did not walk until the age of three and a half years. Family history negative. Clinical features—kypho-scoliosis with

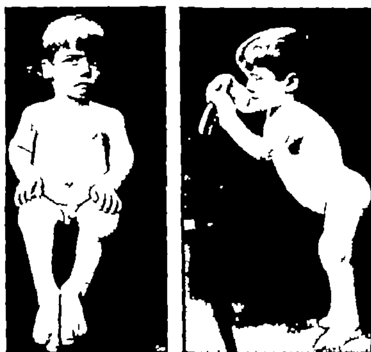


FIG. 171

Case 37—Photographs of the child, aged four and a half years, showing thickening of the ends of the bones and lengthening of the great toes Note the kyphotic curve and the typical standing attitude with the hips and knees flexed.

enormous enlargement of the epiphyses and lengthening of the great toes (an exceptional feature) some limitation of rotation movement at the shoulder joints and of pronation and supination of the forearm Fingers thick and stumpy nails unusually short unable to flex the fingers properly especially at the metacarpo-phalangeal joints. Backward child. Head rather large (Under the late Dr Hugh Thursfield. Reported Thursfield 1925 Fairbank 1927)



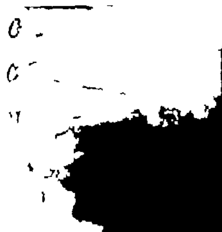


FIG 173

Case 57—Lateral radiograph showing increased antero-posterior measurement of the bodies disc spaces not unduly wide no abrupt kyphos at the dorso-lumbar junction.

FIG 172

Case 57—Upper limb, showing the long bones with enlarged ends and some irregularity of ossification of the epiphyses.



FIG. 174

Case 57—Enlargement of the great toes with irregular ossification at both ends of the first metatarsals and the proximal phalanges.

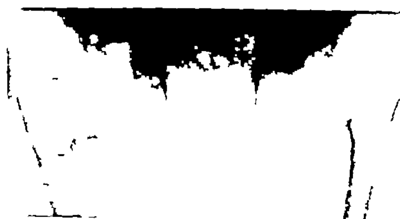


FIG. 175

Case 5 —Showing pe-lik shape of the pelvis poorl dev loped acetabula and marked oxa ara with delayed and irregular ossification of the femoral heads.

CASE 58—CHONDRO-OSTEO-DYSTROPHY (Morquio-Brailsford Type)

(Figs. 176 to 178) Girl aged six years. Sent to hospital for deformity of the wrists and spine Family history negative. Head big skull of normal shape premature closure of sutures. Rigidity localised to the dorso-lumbar junction. Femoral heads prominent abduction of the hips not limited Genu valgum. Abduction of the shoulder joints limited to 80 degrees. Extension of the elbow joints slightly limited. Forearms short especially the ulnae supination excessive. Marked hypermobility of the wrist joints in all directions the fingers can easily touch the flexor aspect of forearms. Fingers and thumbs blunt. (Under Mr H L.-C. Wood.)



Fig. 176

Case 58—Spine showing typical shape of the bodies with the central tongue in front. The second lumbar body is small and displaced backwards. The discs are unusually deep.



Fig 177

Case 58—All the long bones are rather short and stout Note shortness of the ulna and tilting of the lower epiphyses of both forearm bones. Pointing of the bases of the metacarpals is not striking in this case.



Fig 178

Case 58—Pelvis and hip joints, showing pe like shape of the pelvis, large acetabula and only slight irregularity in the ossification of the femoral heads.

CASE 59—CHONDRO-OSTEO-DYSTROPHY (Morquio–Brailsford type)

(Figs. 179 to 183) Boy aged nine and three-quarter years. Deformity of the left hand, suggestive of rheumatoid arthritis since birth. Other deformities not noticed until the age of three or four years. One sister was said to have deformities of the spine and hip joints three other sisters normal Dwarfed Flat depressed nose forehead prominent. Teeth hypoplastic. All epiphyses enlarged and joint movements restricted Complains of lumbar pain when the hip joints are flexed beyond 70 degrees. General muscular weakness. Blood investigations negative, but said to have had negative calcium balance treated successfully with calcium gluconate and vitamin D Marked kyphotic curve with angular accentuation at the dorso-lumbar junction the twelfth dorsal body being small and displaced backwards. Marked changes in the head and neck of both femora no subluxation. Irregular ossification in the epiphyses of the upper end of the tibia, lower end of the humerus (capitellum and medial epicondyle) lower end of the ulna and upper end of both humeri (Under the late Dr Gordon Pugh.)

When examined at the age of fifteen years there was marked kyphosis with a short lordosis below which had improved his general posture genu valgum feet flat general laxity of the knees ankles fingers and particularly the wrists feet blue and cold. Skull broad forehead prominent Teeth good. The outline of the vertebral bodies is now much more irregular in both antero-posterior and lateral films and there is further destructive change in both femoral heads which are now subluxated. (Under the late Sir Henry Gauvain.)



FIG 179

Case 59 at the age of nine years—Radiograph of the spine shows typical tongued vertebral bodies The twelfth dorsal vertebra is reduced in size and is the apex of an angular kyphosis The second lumbar body approximates more closely in shape to the twelfth dorsal than do the others the eleventh dorsal body is slightly smaller than the bodies below it The discs are deep



FIG. 180

Case 59 at 9 years—showing mottling and fragmentation of the capitellum and internal epicondyle of the humerus.



FIG 181

Case 59 at 9 years—showing irregular ossification of the outer part of the tibial epiphysis.



Fig 182

Case 59 t the age of nine years—Radiographs of the pelvis and hip joints show that the pelvis is narrow and there is fragmentation and destruction of the femoral heads w th thickening of the femoral necks. The acetabula are large and poorly formed.



Fig. 183

Case 59 t the ge o The pelvis and f nres in the femoral heads now w th defad f both hip joints at the ge of ne years (Fig 182

CASE 40—CHONDRO-OSTEO-DYSTROPHY (Morquio-Brailsford type)

(Figs. 184 to 187) Girl aged five years Unwilling to walk far cried with pain. Enlarged joints and round shoulders since infancy Father s mother and sister both of short stature (both dead) Stiffness of the shoulder elbow wrist hip and knee joints some limitation of pronation and supination of the forearms. Valgus deformity of feet Blood examination showed nothing of significance General dwarfism limbs more affected than trunk. Moderate kyphosis. Little movement in the spine except in the cervical region. Bridge of the nose sunken. Forehead prominent Long bones stout with splayed ends. When the child is standing the finger tips reach just below the greater trochanters.



Fig. 184



Fig. 185

Case 40 Fig. 184 shows the condition of the spine at the age of two years note the shape of the vertebral bodies the deep disc spaces and the enlargement of the anterior ends of the ribs Fig. 185 shows the condition at the age of five years there are irregularities in outline of vertebral bodies in the lumbar region the appearance suggests that less dense bone has been added above and below the rather denser bodies previously present.



Fig. 186
Case 60 t the age of two years—Radiograph of the pelvis and hip joints shows rather large acetabula and, for this age normally ossified though rather small centres for the femoral heads



Fig. 187
Case 60 at the age of five years—The pelvis and hip joints show progressive changes that were not present t the age of tw years (Fig 186) Thickening of the cortex now seen on the lateral aspect of both femoral shafts is not believed to be significant

GARGOYLISM

Synonyms—Hurler's syndrome, Dysostosis multiplex

This type of chondro-osteo-dystrophy is characterised not only by dwarfism but also by a heavy ugly facies corneal opacity mental deficiency kyphosis distension of the abdomen and enlargement of the liver and spleen. The first two cases were reported by C. Hunter in 1917 the patients were brothers neither had the corneal opacities that are so often a striking feature It is to Hurler that priority of description is often given. She published two cases in 1919 both boys one was investigated later by Tuthill (1934) who first published a detailed account of the neuropathology In 1933 Binswanger and Ullrich reported two cases and suggested the name dysostosis multiplex. In 1936 Ellis Sheldon and Capon in a valuable contribution reported seven cases and reviewed eight others previously published they proposed the title gargoylism and suggested the possibility that a metabolic error might be responsible Many other cases have since been reported. For this review fifty reported cases have been selected. *Hereditary and familial influences*—There is little evidence that heredity plays any part but familial influences are common. Familial incidence was a feature in thirty two of sixty two cases collected by Henderson (1940)

Sex—Both sexes are affected males more often than females in the proportion of four to three.

Age—Only three of the cases studied were under twelve months of age the youngest being eight months but 87 per cent. were under ten years. Few lived until growth was complete

Etiology—It is now agreed fairly generally that this condition must be classified with the lipoidoses although endocrine dysfunction has also been suggested as an explanation of the somewhat complicated pathology which is characterised by changes in so many different tissues Henderson (1940) remarked that hypothalamic disturbances are probably connected with the changes seen in the pituitary and thyroid glands and these in turn with some of the clinical features of the disease such as chondrodystrophy and dwarfism. He agreed with Ellis (1937) that it is yet too early to assess the part played by the thyro-pituitary mechanism. It is difficult to see how metabolic or endocrine error could account for the curious shape of vertebral bodies and still less for local deformity of the spine. Engel (1940) attributed the hypophyseal dysfunction to blebs " caused by escape of cerebrospinal fluid into the adjacent tissues in early embryonic life He included in the bleb diseases a group of ten different syndromes It seems probable that the fault exists at birth but we have found only three reported cases that were recognised in the first year of life

Clinical signs—At birth the size and weight of the child is often above the average but after the first year growth is restricted and there is usually though not invariably increasing evidence of dwarfism There is some degree of micromelia In a well-marked case the head is large the eyes are wide apart sometimes suggesting hypertelorism the bridge of the nose is depressed and the general facies is heavy and ugly There may be prominence of the supraorbital ridges bulging of the temporal regions and ridges along the sutures and around the anterior fontanelles. Scaphocephaly acrocephaly oxycephaly and brachycephaly have all been noted (Ellis *et al* 1936) Hydrocephalus occurs in more than one-third of cases The lips are everted the mouth open and the tongue enlarged so that many are suspected of cretinism. In one patient there were fissures of the tongue and prominent papillae as in a mongol (Ashby *et al* 1937) The mandible is often large The eyebrows are coarse dark and bushy but the hair is usually fine and silky The ears are set low on the head Nasal discharge is frequent Dentition may be irregular and delayed. Cloudiness of the cornea is a striking feature and from the diagnostic point of view important it is caused by multiple opacities in the deeper layers of the cornea. There may be lateral nystagmus (Slot and Burgess 1938) Buphthalmos has sometimes been reported. Optic atrophy occurred in two siblings reported by Davis and Currier (1934) and there is sometimes deafness.

There is often but not always mental deficiency In some patients it has been noted that there was gradual mental deterioration in the course of a number of years. One girl



FIG. 186

Case 60 at the age of two years—Radiograph of the pelvis and hip joints shows rather large acetabula and, for this age, normally ossified though rather small centres for the femoral heads.



FIG. 187

Case 60 at the age of [illegible] years—The pelvis and hip joints show progressive changes that were not present at the age of two years (Fig. 186). Thickening of the cortex now seen on the lateral aspect of both femoral shafts is not believed to be significant.

GARGOYLISM

Synonyms—Hurler's syndrome Dysostosis multiplex

This type of chondro-osteo-dystrophy is characterised not only by dwarfism but also by a heavy ugly facies corneal opacity mental deficiency kyphosis distension of the abdomen and enlargement of the liver and spleen. The first two cases were reported by C. Hunter in 1917 the patients were brothers neither had the corneal opacities that are so often a striking feature It is to Hurler that priority of description is often given. She published two cases in 1919 both boys one was investigated later by Tuthill (1934) who first published a detailed account of the neuropathology In 1933 Binswanger and Ullrich reported two cases and suggested the name dysostosis multiplex. In 1936 Ellis Sheldon and Capon, in a valuable contribution reported seven cases and reviewed eight others previously published they proposed the title gargoylism and suggested the possibility that a metabolic error might be responsible Many other cases have since been reported. For this review fifty reported cases have been selected. *Hereditary and familial influences*—There is little evidence that heredity plays any part but familial influences are common. Familial incidence was a feature in thirty two of sixty two cases collected by Henderson (1940)

Sex—Both sexes are affected males more often than females in the proportion of four to three

Age—Only three of the cases studied were under twelve months of age the youngest being eight months but 87 per cent. were under ten years. Few lived until growth was complete

Etiology—It is now agreed fairly generally that this condition must be classified with the lipoidoses although endocrine dysfunction has also been suggested as an explanation of the somewhat complicated pathology which is characterised by changes in so many different tissues. Henderson (1940) remarked that hypothalamic disturbances are probably connected with the changes seen in the pituitary and thyroid glands and these in turn with some of the clinical features of the disease such as chondrodystrophy and dwarfism. He agreed with Ellis (1937) that it is yet too early to assess the part played by the thyro-pituitary mechanism It is difficult to see how metabolic or endocrine error could account for the curious shape of vertebral bodies and still less for local deformity of the spine Engel (1940) attributed the hypophysial dysfunction to blebs caused by escape of cerebrospinal fluid into the adjacent tissues in early embryonic life He included in the bleb diseases a group of ten different syndromes It seems probable that the fault exists at birth but we have found only three reported cases that were recognised in the first year of life

Clinical signs—At birth the size and weight of the child is often above the average but after the first year growth is restricted and there is usually though not invariably increasing evidence of dwarfism There is some degree of micromelia. In a well-marked case the head is large the eyes are wide apart sometimes suggesting hypertelorism the bridge of the nose is depressed and the general facies is heavy and ugly There may be prominence of the supra-orbital ridges bulging of the temporal regions and ridges along the sutures and around the anterior fontanelles. Scaphocephaly acrocephaly oxycephaly and brachycephaly have all been noted (Ellis *et al* 1936) Hydrocephalus occurs in more than one-third of cases The lips are everted the mouth open and the tongue enlarged so that many are suspected of cretinism In one patient there were fissures of the tongue and prominent papillae as in a mongol (Ashby *et al* 1937) The mandible is often large The eyebrows are coarse dark and bushy but the hair is usually fine and silky The ears are set low on the head. Nasal discharge is frequent Dentition may be irregular and delayed. Cloudiness of the cornea is a striking feature and from the diagnostic point of view important it is caused by multiple opacities in the deeper layers of the cornea. There may be lateral nystagmus (Slot and Burgess 1938) Buphthalmos has sometimes been reported. Optic atrophy occurred in two siblings reported by Davis and Currier (1934) and there is sometimes deafness.

There is often but not always mental deficiency In some patients it has been noted that there was gradual mental deterioration in the course of a number of years. One girl

aged eighteen years showed a very marked degree of statural mental and sexual infantilism (Ellis *et al* 1936) The neck appears to be short and the shoulders are high. Sometimes the deformity of the shoulders almost warrants the title of "congenital elevation of the scapula" (commonly but quite unjustifiably known as "Sprengel's shoulder") The clavicles may be thick. As a rule there is marked kyphosis, angular in shape in the dorso-lumbar region. *There is seldom scoliosis or pigeon-breast* The abdomen is distended to an even greater extent than could be accounted for by enlargement of the liver and spleen which is an important feature in most cases. The liver is more often enlarged than the spleen both being smooth and firm on palpation Quite often there are umbilical and inguinal herniae

There is often limitation of movement of some joints and occasionally of all joints (Davis and Currier 1934 Ellis *et al* 1936) The upper limbs are more often affected than the lower limbs and in the shoulders elbows, and particularly the fingers there is not only limitation of movement but also flexion contracture. Claw hand was regarded as an important feature by Ashby *et al* (1937) The fingers may be short and the ring and little fingers incurved. There may be limitation of extension of the knee joint genu valgum genu varum or flat foot The epiphyses are not enlarged as they so often are in the Morquio-Brailsford group Sometimes even in members of the same family one patient may show all features of the syndrome while another shows only bone changes (Ellis *et al* 1936)

Blood examination reveals nothing of importance. Biochemical studies have shown no constant abnormality

Radiographic appearances—The radiographic appearances in gargoylism show general resemblance to the changes that are seen in Morquio-Brailsford disease but there are distinct differences in the skull the vertebrae and the hip joints.

The skull—Most cases of gargoylism show enlargement of the sella turcica even to twice the normal size with or without hydrocephalus. There is no evidence of erosion and it has been suggested that this enlargement is due to malformation of the sphenoid rather than to abnormality of the pituitary gland or increased intra-cranial pressure (Ellis *et al* 1936)

The spine—In the spine the upper and lower surfaces of the vertebral bodies are convex so that they present a circular rather than a quadrilateral outline the discs are biconcave and deeper than normal. It is often said that the bodies are spread and flat as in the Morquio-Brailsford type but this is not accurate When there is angular kyphosis—and this occurs with far greater frequency than in the Morquio-Brailsford type—one body is usually smaller than the others and is displaced backwards as if squeezed out of line. The mal alignment is always more obvious above the small body than below it the vertebrae above appear to have slipped forwards on the small deformed body This deformity is seen in both types of chondro-osteo-dystrophy but there is no other resemblance The displaced vertebral body is concave on its anterior surface the upper part being deficient and the lower part projecting forwards in the form of a beak. This beak is quite different both in shape and position from the central "tongue" seen in the Morquio-Brailsford type The typical shape and displacement is seen most often in the second lumbar vertebra and, next in frequency in the first lumbar vertebra in only one case was the twelfth dorsal as well as the first lumbar vertebra small beaked and displaced A similarly peculiar shape is often seen in the vertebral body next below the one displaced and occasionally in the one above it This distortion which is a diagnostic feature is usually seen only in two or three of the upper lumbar bodies but in two patients the first four lumbar bodies were all affected In one patient the fifth lumbar vertebra showed typical deformity in this case the first and second bodies and possibly the fourth were also affected but the third lumbar vertebra was normal Only one case has been found in which the shape of the bodies as seen in lateral radiographs failed to indicate clearly to which group of chondro-osteo-dystrophy the case belonged (Snoke 1933) If lateral radiographs are taken when the spine is flexed it will be seen that much more movement takes place at the level of the disc above the small body than in the disc below

CASE 61—GARGOYLISM

(Figs. 188 to 192.) Male aged two and a half years. Deformity of chest noticed at nine months becoming worse. Kyphosis present at eleven months. Head large facies heavy Backward but no gross mental deficiency squints. Limitation of movement of some joints especially the shoulders. Hands spade-like fingers curved. Stands with hips and knees flexed. Knock knee No corneal opacities. Liver and spleen not enlarged. Umbilical and left inguinal herniae. Radiographs sella enlarged spine typical of gargoylism with lumbar kyphosis clubbing of lower ribs bilateral coxa valga metacarpals of typical shape. Two other children both normal. (Under Mr Eric Lloyd.)





FIG. 188

Case 61—Photographs showing the large head and typical heavy features. Note the typical attitude on standing with the hips and knees flexed, and the lumbar kyphosis.



FIG 189



FIG. 190

Case 61—Showing enlargement of the sella turcica (Fig 189) and enlarged acetabula, poorly formed roof and a mild degree of coxa valga (Fig 190).



Fig. 191



Fig. 192

Case 61. Lateral radiograph of the spine (Fig. 191) showing the apex of the kyphosis formed by the second lumbar body which is small (D 1 is without corresponding ribs). The bodies of the second and third lumbar vertebrae show beaked shape. There is some enlargement of the anterior parts of the ribs. Lateral radiographs of the spine taken in flexion (Fig. 192) show that there is much greater forward movement of the first lumbar vertebra, occurring at the intervertebral joint between it and the small displaced second lumbar body than at any other level of the spine.

CASE 62—GARGOYLISM

(Figs. 193 to 196) Male aged three years. Mentally backward. Corneae cloudy Facies coarse and heavy Head large bossing above ears eyes widely separated bridge of nose broad teeth spaced hair coarse eyebrows thick. Liver and spleen enlarged. Nasal discharge. Unable to sit up Well-defined angular kyphosis in upper lumbar region. Some scoliosis. Limitation of movement of the elbows. Radiographs coxa valga femoral necks long acetabular roofs sloping skull large pituitary fossa enlarged antero-posteriorly no sign of erosion second lumbar body rather small, of typical shape and slightly displaced backwards other bodies biconvex. Biochemical investigations revealed nothing of importance (Under Dr Wilfred Sheldon.)



Fig. 193



Fig. 194

Case 62—Lateral radiograph of the skull (Fig 193) shows the abnormal size of the sella turcica, which has a smooth, sharply defined outline Radiograph of the hand (Fig 194) shows the abnormal shape and texture f the bones The bases of the metacarpals are somewhat pointed. The radius and ulna re thick and the lower ends of their shafts deformed.



Fig 195



Fig. 196

Case 62—The roof of the acetabulum s poorly formed on both sides nd the femoral heads lie a little high (Fig 195) There is bilateral coxa alga and the femoral necks are of unusual length. Radiograph of the spine (Fig 196) shows an angular deformity with the pex t the second lumbar ertebra, the body of which is small, beaked and displaced a little backward. The other ertebral bodies are biconvex and not flattened.

CASE 63—GARGOYLISM

(Figs. 197 to 200) Male aged nine years Mentally backward but talkative and observant Walked at the age of one year Noticed to be clumsy with his hands at the age of two years. Definitely dwarfed. Head not unduly large One eye removed for glioma of retina. Spleen just palpable liver not enlarged. Some limitation of movement of the shoulder elbow hip and knee joints. Fingers short and stubby joints thick extension limited. The three inner fingers curve towards the first. Bones of the arms forearms, and wrists feel thicker than normal. Radiographs sella small long bones thickened coxa valga acetabula of better shape than usual spine typical. *Blood examination* nothing of significance He is the seventh of a family of seven the eldest being twenty-eight. (Under Dr E. A Cockayne)

Figs. 197 and 198

Case 63—Photograph of the child at the age of nine years (Fig. 197) shows that the face is by no means typical. The arms are rather short. Radiographs of the skull showed a small sella turcica and no signs of frontal sinuses which should be visible at this age The spine (Fig. 198) shows biconvex bodies, the second lumbar being rather small and of typical beaked shape a suspicion of a similar shape is seen in the third and fourth lumbar bodies.



Fig. 197



Fig. 198

Figs. 199 and 200

Case 63—The right forearm (Fig. 199) shows stout bones, impaired ossification of the lower radial and ulnar epiphyses and of the carpus, and abnormal shape and texture of the bones of the hand Note the tilting of the lower end of the radius and ulna The femora show unusual thickness (Fig. 200) The symmetrical thickening of the lateral cortex is curious but is not regarded as significant similar thickening has been seen in a case of chondro-osteo-dystrophy of the Morquio-Brailsford type



Fig. 199

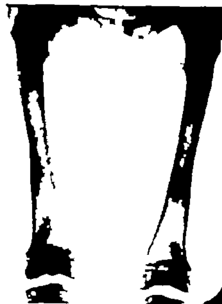


Fig. 200

CHAPTER 13

ACHONDROPLASIA

Synonyms—Chondrodystrophia foetalis, Micromelia

Achondroplasia is a congenital condition resulting from interference with enchondral ossification and is characterised by dwarfism of the short limb type associated with a large head and in many cases, so-called trident hands. It is the commonest type of dwarfism and perhaps the most ancient there is clear evidence of its existence several thousand years ago. Although he was not the first to recognise that this affection was distinct from rickets, it was Parrot (1878) who suggested the descriptive title achondroplasia. The term chondrodystrophia foetalis was suggested by Kaufmann in 1892 Even in recent years many cases have been reported as examples of achondroplasia which really belong to the chondro-osteo-dystrophy group while numerous atypical" cases have been published which at present it is impossible to classify

As to its frequency Caffey (1948) reported that at the Babies Hospital in New York City forty-three achondroplasiacs were identified radiologically in the course of fifteen years in the same period there were fifteen cases of osteogenesis imperfecta fourteen ateleiotic dwarfs, ten cases of gargoylism and nine of multiple exostoses (diaphysial aclasis) Achondroplasia undoubtedly occurs in certain animals but it is no longer regarded as a satisfactory explanation for the stunting of limb-growth in all short-limbed species. A lethal form of the disease has been reported in rabbits (Brown and Pearce 1945)

Hereditary and familial influences—These are apparent only in a minority of cases but achondroplasia has been traced through as many as six generations in the male line (Phemister 1924) Most cases—nearly 90 per cent. of the series studied by Mörch (1941)—are sporadic. Nevertheless there is a 50 per cent. chance that a child, one of whose parents is an achondroplastic dwarf will also be affected. Difficulties in labour in the female achondroplasiac interfere with inheritance. It has been met with in twins, one or both being affected.

Sex—Females are rather more frequently affected than males. Rischbieth and Barrington (1912) found seventy females and fifty six males in the series they investigated.

Age—The characteristics are present at birth whereas in cretinism and chondro-osteo-dystrophy the special features including the dwarfism, develop after birth. It is usually said that most die before at or soon after birth, which is often premature at about the eighth month. The maternity hospital records examined by Mörch showed that 80 per cent of affected children died during the first year of life. In view of these statements it is curious that the patients that survive are so singularly sturdy and robust and that they live to an advanced age

Etiology—Achondroplasia results from a developmental fault inherent in the ovum, the cause of which is entirely unknown. Of the various explanations that have been suggested none has received general acceptance The failure of normal ossification of the long bones is apparent in the foetus towards the end of the second month or early in the third month of foetal life This fact and the occurrence of the condition in only one of a pair of twins eliminates the possibility of an endocrine error as the cause It affects all races and as already mentioned, it occurred in prehistoric times. This is one of the conditions which Jansen (1912) suggested were the result of excessive intra-uterine pressure caused either by hydramnios or a small amnion but if this is true how is it that most cases are so singularly true to type?

Clinical features—These are obvious at birth whether the child is alive or dead Dwarfism is the most striking feature the reduction in height being due chiefly to shortness of the lower limbs. When adult life is reached and growth ceases the height is usually less than four feet and may be as little as two feet six inches. The mid-point of stature is always above

the umbilicus and may be as high as the lower end of the sternum. Although the spine is affected to some extent the limbs are strikingly short in comparison with the trunk. The fingers may not reach below the greater trochanters. The shortness of the lower limbs may enable a child to kiss his toes with ease when standing The proximal segments of the limbs —the humeri and femora—are more affected than the distal segments (rhizomelic micromelia) The head is large and brachycephalic, and suggestive of hydrocephalus which may be present in mild degree though it is not progressive (Dandy 1921) The frontal region is rather prominent and the bridge of the nose is depressed and flattened. The lips are often thick and during the early months of life the tongue may protrude. The mandible may be somewhat prognathous. Dentition is normal The spine may be lordotic but is often surprisingly flat the apparent lordosis being due more to the unusual prominence of the buttocks than to excessive curvature of the lumbar spine This deformity does not flatten out as the child is laid on its back not even when the hips are fully flexed There may be a kyphotic curve in the dorsal region. The chest is small and flat the ribs being abnormally short with perhaps some beading at their anterior extremities (Parsons 1936) the costal cartilages are unaffected. The breadth of the shoulders is up to the average. Movements of the shoulder joints and supination of the forearms may be somewhat limited (Caffey 1948) Fixed abduction of the upper limbs with limitation of adduction, has been reported. Extension of the elbows may be limited in one case examined extension was checked at 120 degrees.

The hands are short and broad and frequently but not invariably they display a typical deformity The middle finger is short and the fingers are more nearly of equal length than in a normal hand. The digits which are all rather short and thick diverge the space between the second and third fingers being particularly wide thus is formed the main en trident of Marie (1900) The legs are often bowed except in younger children in whom they are usually straight and even occasionally valgoid. The bowing associated in some cases with hyperextension of the knees is due mainly to curvature of the tibiae the deformity occurring usually but not invariably in the upper part of these bones. Correction of deformity by osteotomy may be justifiable but is seldom necessary The head of the fibula lies abnormally high The general appearance of the limbs is one of sturdiness with some enlargement of the ends of the bones. The musculature is often above the average these patients may perform feats of strength and be able to rise from the floor in one movement (Parsons 1936) The gait is rolling—probably because of the backward tilt of the pelvis and the posterior displacement of the hip joints It is certainly not due to coxa vara, though it is often stated quite incorrectly that this deformity is always present

The skin is thick and the soft tissues generally seem to be too long for the limbs so that in younger children folds and furrows are formed between rolls of fat The abdomen is rather large and prominent Intelligence is normal but the subjects of achondroplasia may be affected psychologically by their difference from other children or by the curiosity they invoke if they join a performing troupe Sexual development is normal, or it may be somewhat excessive

Although in most cases the whole skeleton is affected, the impairment of growth is occasionally of a more limited distribution exceptionally the dwarfism is even confined to one limb The author has seen a woman with both humeri dwarfed to a marked degree while the forearms lower limbs head and body were all of normal size

Blood examination reveals nothing abnormal.

Radiographic appearances—The long bones are short strong and rather dense The femora and humeri may be less than two-thirds of the normal length. The curves and muscular impressions are exaggerated. The shafts may be thickened but usually the increase in diameter is more apparent than real and is due to the reduction in length. The *medullary* canal is reduced in size and may be obliterated by cancellous bone Splaying of the ends of the shaft is more abrupt and obvious than in normal bones and the terminal surface is irregular In some of the major long bones notably in the region of the knee joint the end

of the shaft is notched centrally to form a V-shaped surface The epiphyses appear to be large but as a rule they are not abnormal in size They may begin to ossify somewhat early while fusion with the shafts shows great variation occurring either early late or at the normal time. A striking feature is the position of the epiphysial centre close to the end of the shaft and tucked into the apex of the V-shaped notch of the metaphysis when this is present. The two limbs of the notch may appear to embrace the epiphysis—an impression that is confirmed by histological examination In young children the position of the epiphysial centre so close to the diaphysis results in considerable increase in depth of the joint space as seen in radiographs (Fairbank 1934) In a stillborn infant there may be such shortness of the diaphyses that more than half the length of the limb is formed by the epiphyses (Khoo 1945) The clavicles and fibulae are much less affected than other long bones The relative excess in length of the fibula may be regarded as a persistence of the condition that is said to be present normally at the eighth month of foetal life. The fibular head lies higher than usual occasionally it may even participate in the formation of the knee joint. Sometimes the shaft of the fibula is bowed. The ulna on the other hand, is occasionally shorter than the radius, as it may be in several other general affections of the skeleton. The ribs are short—sometimes even less than half the normal length. The sternum is short broad and thick, and the sternal angle is increased The scapula is deformed, its shape suggesting that the inferior angle has been cut off and the glenoid is too small for the humeral head. The pelvis is reduced in size in all diameters. The ilium, especially in adults, is small and the crest is thickened. In children the lower part of the ilium, above the acetabulum, is broader than normal and the bone as a whole is of a curious shape. The hip joint lies farther back than usual, so that the acetabulum abuts on the sacro-sciatic notch Sometimes the pubic arch is unusually wide. The sacrum is narrow and tilted to an abnormal degree its promontory protruding more than usual into the pelvic cavity Coxa vara is often stated to be common even invariably present but this is not supported by examination of radiographs.

The skull is large the sella may be small. The characteristic feature is premature fusion of the pre-sphenoid post-sphenoid and basi-occipital to form an os tri-basilare which is abnormally short As a result there is considerable diminution in length of the base of the skull The foramen magnum is small and funnel-shaped its diameter may be reduced to half the normal. The facial bones are unaffected. The vertebral bodies may be somewhat reduced in depth but the total reduction in length of the spine is much less marked than that of the limbs. Reduction in size of the ossific centres for the vertebral bodies was regarded as a constant feature by Parrot (1878) but the bodies are never noticeably shallow and the kyphotic curve is long and gradual. Nevertheless angular kyphosis suggestive of that met with in the two types of chondro-osteo-dystrophy was seen in two undoubted cases of achondroplasia examined by the author In one patient only two years old the deformity almost disappeared on standing

Progress—Even when fusion of the epiphyses is delayed adults are always far below the normal in height

Pathology—There is relative aplasia of cartilage at the ends of the long bones. Growth of all cartilage cells of the epiphyses is disorderly According to Harris (1933) mucoid degeneration of the cartilage is the underlying feature It may be degenerate fibrillar vacuolated and unusually vascular There is absence of the normal columnar palisade arrangement at the epiphysial line and provisional calcification is erratic. The spongiosa is irregular and tends to be dense with the cartilage cores diminished in calibre or entirely absent (Caffey 1948) Harris regards the shafts as the serial summation of lines of arrested growth Periosteal ossification is normal or excessive The periosteal ferrule outstrips and overlaps the cartilage-formed bone (Keith 1910) This explains the radiographic appearances in which it was noted that the cortex of the metaphysis appears to embrace the adjacent part of the epiphysis An important feature oft t invariably present is the ingrowth

from the periosteum of a vascular fibrous band or layer between the zone of ossifying cartilage at the epiphysial line and the rest of the epiphysis if as occasionally happens this fibrous layer extends across the whole diameter of the bone further growth of the shaft must necessarily cease. According to Knaggs (1927) this band may be formed by metaplasia of the cartilage The thymus, thyroid and pituitary show no constant changes.

Death at or shortly after birth is attributed either to the inadequate capacity of the thorax or to excessive reduction in the size of the foramen magnum. It has been said that general oedema and ascites may cause difficulty at birth

Diagnosis—Achondroplasiacs display their typical features at birth whereas infants with either of the two types of chondro-osteo-dystrophy usually pass as normal for the first one to four years of post natal life and owe their dwarfism to the spine rather than to the limbs moreover in these dwarfs kyphosis, rather than apparent lordosis, is the rule In the Morquio-Brailsford type of chondro-osteo-dystrophy the head and face are normal while gargoylism is distinguished by the heavy facies, mental deficiency corneal opacities, and enlargement of the liver and spleen. In cretinism the characteristic features are not recognisable at birth The only condition that is likely to simulate achondroplasia at birth is osteogenesis imperfecta in a severe pre-natal case of this condition, the subject whether alive or dead at birth may display marked shortening of the limbs as compared with the trunk but radiographic examination at once settles any doubts as to the diagnosis. Short limbs at birth may also be seen in dysplasia epiphysialis punctata but this is an exceedingly rare condition with unique radiographic features.



Fig. 201

Case 64—Typical achondroplasia in a female infant. Note that the dwarfism is due chiefly to shortness of the lower limbs —not the trunk. The mid-point of stature is at the lower end of the sternum. The fingers reach only t the greater trochanters. The soft tissues of the limbs are too long for the bones so that there re many cutaneous creases and rolls of fat.

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CASE 65—ACHONDROPLASIA

(Figs. 202 to 206.) Male aged seven years. Typical case. Some limitation of extension of the hips. Extension of the elbow joints limited. Subluxation of the head of the radius particularly in the left elbow; the subluxation occurs on flexion, the radial head resuming an approximately normal position on extension. Outer ends of clavicles bent down. (Under Dr R. S. Frew.)

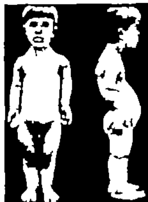


Fig. 202

Figs. 202 and 203

Case 65—Typical short-limbed dwarf (Fig. 202) with large head, prominent forehead, depressed bridge of nose, small flat chest and prominent abdomen, long dorso-lumbar kyphosis with minimal true lordosis but with prominent buttocks, and relative shortness of all four limbs, particularly the proximal segments (rhizomelic micromelia). Figure 203 shows the unusual shape of the ilia, and the absence of coxa vara though the femoral necks are prolonged inwards at the epiphyseal lines. Note the short femoral shafts, splayed at the extremities, particularly the lower which show the typical central notches into which the epiphyses fit.



Fig. 203



Fig. 204

Case 65—Hands showing typical trident deformity and thick digits.





Fig. 205



Fig. 206

Case 65—Note the marked splaying of the metaphyses of the femora and tibiae (Fig. 205), the central notches particularly in the femora, the close proximity of the epiphyses to their respective shafts, and the wide joint space in both knees. The upper limb (Fig. 206) shows the stout shaft of the humerus with an unusual shape of the extremities of the bone. The radial head is in an approximately normal position, the elbow being extended to the limit.

CASE 66—ACHONDROPLASIA

(Fig 207) Female child aged seven months who displayed all the features of achondroplasia There was some asymmetry both upper limbs were relatively short as also were the lower limbs but the left upper limb was shorter than the right. The head was large There were trident hands with pointed fingers. There was a low dorsal kyphosis. (Under Dr R. S Frew)



FIG. 207

Case 66—Radiograph of the leg shows the position of the epiphysial centres in the region of the knee joint, close to the ends of the shafts and not in the middle of the cartilaginous epiphyses Note the apparent widening of joint spaces.

FIG. 207

CASE 67—ACHONDROPLASIA

(Figs. 208 and 209) Female aged five years. Typical case.



FIG. 208

Case 67—Lower limbs showing the typical short stout bones with splaying at the extremities, irregularity of the ends of the metaphyses, and characteristic position of the ossific centres Note the length of the fibula the head is abnormally high in both legs at the [illegible] joint the fibula reaches rather lower than usual.



Fig. 209

Case 67—Pelvis and hips showing the same curious shape of the ilia as seen in Figure 203. Note the flat horizontal roof of the acetabulum on both sides. The femoral necks show some lipping on the inner side but are not varoid.

CASE 68—ACHONDROPLASIA

(Figs. 210 and 211.) Female, aged five and a half years. Typical case clinically and radiographically except that the spine displays deformity that is suggestive of the chondro-osteo-dystrophies. (Under the late Sir Henry Gauvain.)



Fig. 210



Fig. 211

Case 68—Photograph shows the typical features of achondroplasia (Fig. 210). The lateral view of the spine shows the twelfth dorsal body slightly wedge-shaped, forming the apex of an angular kyphosis. Note that the shape of the vertebral bodies differs both from that seen in the Morquio-Brailsford syndrome and from that typical of gargoylism.

CASE 69—ACHONDROPLASIA

(Figs. 212 to 214.) Female aged two years. Below normal height for her age. Relative shortness of the limbs especially the proximal segments. Head large; facies not typical. Intelligence normal. Hands trident. Slight limitation of extension of the elbow joints. Angular kyphosis of the spine with apex at dorso-lumbar junction; on standing the kyphosis almost disappears. Radiographic appearance of long bones and of ilia is typical of achondroplasia. The lower ends of the scapulae are square as if the angles had been cut off.



FIG. 212
Case 69—Thorax and shoulders with arms elevated to show the curious square "angles" of the scapulae.



FIG. 213



FIG. 214

Case 69—Pelvis and lower limbs showing the typical shape of the ilia, femora and tibiae (Fig. 213). Lateral view of the spine shows angular kyphosis at the first-second lumbar level but without features typical of either type of chondro-osteo-dystrophy.



FIG 209

Case 67—Pelvis and hips showing the same curious shape of the ilia as seen in Figure 203 Note the flat horizontal roof of the acetabulum on both sides. The femoral necks show some lipping on the inner side but are not varoid.

CASE 68—ACHONDROPLASIA

(Figs. 210 and 211) Female aged five and a half years. Typical case clinically and radiographically except that the spine displays deformity that is suggestive of the chondro-osteo-dystrophies (Under the late Sir Henry Gauvain.)





FIG 210 FIG 211

Case 68—Photograph shows the typical features of achondroplasia (Fig 210) The lateral view of the spine shows the twelfth dorsal body slightly wedge-shaped, forming the apex of an angular kyphosis Note that the shape of the vertebral bodies differs both from that seen in the Morquio-Brailsford syndrome and from that typical of gargoylism.

CASE 69—ACHONDROPLASIA

(Figs. 212 to 214) Female aged two years. Below normal height for her age. Relative shortness of the limbs especially the proximal segments. Head large; facies not typical. Intelligence normal. Hands trident. Slight limitation of extension of the elbow joints. Angular kyphosis of the spine with apex at dorso-lumbar junction; on standing the kyphosis almost disappears. Radiographic appearance of long bones and of ilia is typical of achondroplasia. The lower ends of the scapulae are square as if the angles had been cut off.

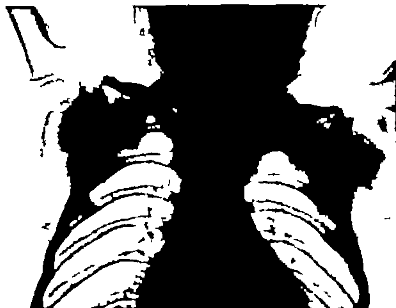


Fig. 212

Case 69—Thorax and shoulders with arms elevated to show the curious "square angles" of the scapulae.



Fig. 213



Fig. 214

Case 69—Pelvis and lower limbs showing the typical shape of the ilia, femora and tibiae (Fig. 213). Lateral view of the spine shows angular kyphosis at the first-second lumbar level but without features typical of either type of chondro-osteo-dystrophy.



Fig. 209

Case 67—Pelvis and hips showing the same curious shape of the ilia as seen in Figure 203. Note the flat horizontal roof of the acetabulum on both sides The femoral necks show some lipping on the inner side but are not varoid.

CASE 68—ACHONDROPLASIA

(Figs. 210 and 211) Female aged five and a half years. Typical case clinically and radiographically except that the spine displays deformity that is suggestive of the chondro-osteo-dystrophies. (Under the late Sir Henry Gauvain.)





Fig. 210 Fig. 211

Case 68—Photograph shows the typical features of achondroplasia (Fig. 210) The lateral view of the spine shows the twelfth dorsal body slightly wedge-shaped, forming the apex of an angular kyphosis Note that the shape of the vertebral bodies differs both from that seen in the Morquio-Brailsford syndrome and from that typical of gargoylism.

CASE 69—ACHONDROPLASIA

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Fig. 212
Case 69—Thorax and shoulders with arms elevated to show the curious square " angles " of the scapulae.





Fig. 213 Fig. 214
Case 69—Pelvis and lower limbs showing the typical shape of the ilia, femora and tibiae (Fig. 213). Lateral view of the spine shows angular kyphosis at the first-second lumbar level but without features typical of either type of chondro-osteo-dystrophy

CHAPTER 14

MYOSITIS OSSIFICANS PROGRESSIVA

Synonyms—Fibrositis Ossificans Progressiva

This congenital affection is characterised by the formation of columns of bone in the soft tissues with progressive limitation of movement. It is usually associated with microdactyly. According to Vastine *et al* (1948) it was von Dusch who named the condition myositis ossificans progressiva in 1868 though cases had been described many years before. This title is unfortunate because the primary change is in the connective tissues, fasciae and tendons, the muscle fibres being affected only secondarily and moreover the changes are not of an inflammatory type. The condition was reviewed by Rosenstirn (1918) who collected 120 cases from the literature in a few of these he rightly questioned the diagnosis and he suggested that "fibro-cellulitis ossificans progressiva" was a more accurate title. The subject was reviewed by Nutt in 1923 and he added fourteen more cases from the literature together with one of his own. It was also reviewed by Mair in 1932. Other titles that have been suggested are "fibrositis ossificans progressiva" (Greig 1931) and "hyperplasia fascialis ossificans progressiva" (Goto 1912, reported by Rosenstirn).

Hereditary and familial influences—There is little evidence of hereditary or familial influence. Sympson (1886) reported a father and son with digital deformity but only the son developed myositis. Drago (1919) reported a patient whose mother had microdactyly. Burton-Fanning (1901) published the case of a father and son both of whom had myositis ossificans. Gaster (1905) reported the affection in a grandfather father and three sons—five cases in three generations. It has also occurred in twins, both of whom developed myositis (Vastine *et al* 1948).

Sex—Both sexes are affected, males more often than females in the proportion of approximately three to two.

Age—It is obvious that microdactyly arises in foetal life but the other manifestations usually develop in childhood before the age of ten years. In about 16 per cent of cases the early signs were noted in the first year of life and, in some striking changes in the muscles have been observed so soon after birth that they must have begun in foetal life (Hutchinson 1860 Rosenstirn 1918 Mair 1932). Only occasionally is the onset delayed until adolescence. Mair (1932) found only two records of cases in which the first symptoms appeared after the age of twenty years (Frejka 1929 Hirsch and Löw-Beer 1920).

Etiology—Maldevelopment of the great toe must begin in early foetal life and the fault that is responsible for changes in the muscles no matter how long their onset may be delayed, is also congenital. The cause of this mesodermal fault is unknown. No error in calcium metabolism has been proved. It has been suggested that the underlying cause may be similar to that which is responsible for local ossification after injury the difference between the two conditions being only one of degree (Painter 1921) but study of the two types of case provides little support for this suggestion. The disorder has been reported in dogs and in at least one instance it was associated with microdactyly (Rosenstirn 1918).

Clinical signs—Severe crippling may supervene within a few years or it may be delayed for three or four decades. In a typical case localised swellings appear during infancy and childhood usually in the region of the head or neck and, sooner or later in the trunk. The swellings may be painful but quite often they are painless and not tender. As a rule they are small lasting only a few days or weeks then subsiding or even disappearing altogether only to be succeeded by others. Injury may sometimes determine the site of a lesion and start the whole

process, but as a rule injury plays no part at all. Garrod (1907) studied a child during the second year of life and described two types of swelling 1) swellings attached to the deep fascia covered with normal and mobile skin firm elastic and not tender with thin processes extending from some of them 2) diffuse ill-defined thickening of the soft parts with adherent skin sometimes with local oedema seen mostly in the lumbar and sacral regions. A swelling that occurred in the neck caused oedema of the arm and dilation of the veins in less than three weeks it had almost disappeared and the head then moved freely A lump might divide into two each part being joined by diffuse swelling and one lump was seen to divide on two separate occasions. In studying a boy aged four years, Mair (1932) found that the swellings might be hard from the beginning and thereafter persist, or they might be cyst-like fluctuant, and blue-red in colour Swellings of the fluctuant type sometimes resolved into firmer lumps or they disappeared altogether apparently these were haematomata. A lump has been known to break down and discharge They vary in size. In a child aged eighteen months a swelling as large as an apple appeared in the neck and disappeared within two months (Westman 1924) In another case there was a swelling the size of an egg which also disappeared. One patient, when four years of age was said to have the appearance of being " contused all over " (Hamada 1936)

The swellings often cause stiffness and inconvenience if not actual discomfort their development may be associated with slight fever even when occurring several months or years after the onset of the disease. Usually the overlying skin is not congested. Even in the early stages there is limitation of movement of the head and neck, often with wry neck deformity or limited movement of one or both arms. If a lump subsides or disappears, freedom of movement may be restored. The masseter is affected in about one-fifth of the cases. Almost invariably the dorsal aspect of the trunk is involved and there may be involvement of the proximal parts of the limbs, particularly the upper limbs. Limitation of movement or complete fixation of the elbow by bone block is not unusual but there is seldom involvement of the limbs distal to the elbows or knees. Lumps have been reported over the sternum

Sooner or later columns, irregular masses or plates of bone appear in the soft tissues. If a lump does not disappear completely bone may be expected to make its appearance within a period of from two to eight months. These bony columns seem to lie in the course of a muscle—for example in the sternomastoid or in the latissimus dorsi or erector spinae but bone may also be laid down in tendons fasciae and ligaments. Sometimes bone is found in unexpected places where it is difficult to decide the tissue in which it has formed for instance there is sometimes a bar of bone passing almost horizontally outwards from a mass in the back of the trunk to be attached to the humerus near the insertion of the deltoid far below the normal position of any muscle inserted into the humeral shaft. The column may be attached to a skeletal bone at one or both ends or it may be entirely free On the back, nodular columns of bone often stand out boldly not uncommonly forming a V with or without a third vertical column in the midline and in such cases the latissimus dorsi and erector spinae muscles are believed to be the sites of the bone formation. The deltoid biceps brachialis anticus and adductor magnus may be affected but with much less frequency The sternohyoid genio-hyoid and sterno-thyroid muscles have sometimes been affected. The skin has been known to ulcerate over a projecting mass of bone as for example in the region of the tuber ischii. Ossification of a tendon near its attachment may produce a form of exostosis In the forearm and leg the interosseous membrane may be involved.

Certain muscles seem to be exempt namely the muscles of the eye face tongue diaphragm heart larynx perineum and the sphincters (Mackinnon 1924 Grant 1919) Bone formation has seldom occurred in the skin or in the abdominal wall (Rosenstirn 1918)

Sooner or later the spine becomes stiff with or without kyphosis or scoliosis. The whole spine including the occipito-atlantal joint may be completely rigid. The costo-vertebral

joints are stiffened and the chest becomes immobile. As a rule the patient is thin and wasted, and in the worst cases he is bedridden. Involvement of the masseter may interfere seriously with feeding and it may even be impossible to open the mouth. The masseter was involved at the early age of three weeks in a child who survived only six months (King 1854) The temporal and frontalis muscles have been affected (Morian 1899) Resistance to general infections is lowered and intercurrent disease is common. Nevertheless some patients have lived to an advanced age.

In the Hunterian collection of the Royal College of Surgeons of England there is the skeleton of a man of thirty-nine years, a full report of which has been studied by courtesy of Dr L. W Proger This specimen shows clearly that bone formation is not confined to the muscles nor even to their immediate vicinity (Fig 11) In the skull many small outgrowths of bone are seen at various sites, including the supra-orbital ridge and the alveolar process of the superior maxilla there is extensive ankylosis of the lateral articulations of the spine and most of the costo-vertebral joints some neural arches are fused and at certain levels, the supraspinous ligaments are ossified. Attached to the back of the left ilium is a perforated shell of bone which bulges outwards as if it had been formed in the subcutaneous tissue of the buttock—certainly not in the gluteus maximus. Passing from the angle of the left scapula to the humerus is a bar of bone which lies so low and so horizontal that it could have no possible connection with the teres major muscle. The carpal and tarsal ligaments are ossified. This skeleton and two others similarly affected, are described by Stonham (1892)

Microdactyly was first recorded by Helferich (1879) and it is of diagnostic importance, particularly in the early stages before heterotopic bone has formed. The great toes are affected in about three-quarters of all cases. Hallux valgus is common and there may be a scar over the metatarsal head. Reduction in length of the thumb is less frequent it occurs in less than half the cases. Other digits are affected exceptionally In two cases all the fingers were reduced in length.

Other changes—In at least two cases the femoral necks were thickened (Rocher *et* Mathey-Cornat 1933 Griffith 1949) Mental and sexual development are normal. There may be some degree of infantilism, presumably secondary but this is exceptional.

Blood chemistry—No constant abnormalities have been found. In the few cases in which blood phosphatase has been estimated it was within normal limits.

Radiographic appearances—The density of the extra-skeletal bone varies considerably it may be less dense and less defined than the normal skeleton or on the other hand it may be more dense the skeleton as a whole being osteoporotic in consequence of the severely restricted activity Exostotic projections or subperiosteal thickenings on the shaft of a bone may be seen in addition to columns of bone in the soft tissues. In an advanced case there may be fusion of vertebrae In one there was such extensive formation of bone in the quadriceps muscle as to suggest that there were two femoral shafts and in another there was a continuous sheet of bone from the quadriceps to the tibia completely fixing the knee (Mair 1932)

Microdactyly is associated with reduced length of the phalanges of the great toe and only exceptionally with a short metatarsal bone there is complete or incomplete suppression of the proximal phalanx which may be reduced to a wedge-shaped fragment It is said that the phalanges are often fused but the evidence of this is not convincing The first metatarsal may actually be increased in length by fusion of part of the proximal phalanx, thus forming a rounded end to the bone quite unlike the normal head. A similar shaping of the head may also be seen when the bone is shorter than normal. In the thumb all three bones may be short, or there may be shortening only of the phalanges. In a case reported by Burrows (1933) the metacarpal was short and the epiphysis of the proximal phalanx was wedge-shaped. Spurs on the back of the os calcis or in front of its tuberosities have been reported. The formation of an exostosis on the phalanx of a finger has been described in two children (Rolleston 1901 Herringham 1898)

Progress—The condition usually becomes progressively worse but the rate of progress varies. Intermissions are not uncommon and sometimes there may be arrest for several years. The time elapsing between the onset of the first symptom and final crippling of the patient may vary from less than ten years to as long as forty years. No treatment is known to arrest the progress of the disease although the possibilities of radiotherapy have not perhaps been fully explored. Operative excision of a bony column is very uncertain in its results it may not improve the mobility of the joint and moreover bone is likely to reform.

Pathology—There seems no doubt that the primary change occurs in the connective tissue and not in the muscle fibres which are affected secondarily Intercellular haemorrhage is succeeded by proliferation of embryonic tissue particularly around the vessels and between the muscle fibres, together with the formation of adult connective tissue cartilage and bone These changes are accompanied by fatty waxy and granular degeneration of muscle fibres and proliferation of the sarcolemma cells (Grant 1919) The new bone is metaplastic and does not depend in any way on the osteoblasts in the adjacent skeleton It may be associated with the formation of cartilage and the bone may be hard or soft but microscopic and chemical examinations have revealed no differences from normal bone

Diagnosis—Before a case has progressed to the formation of bone the diagnosis may be difficult but the co-existence of microdactyly should settle any doubts. Myositis fibrosa a very uncommon condition is no longer universally regarded as a separate affection. It is noteworthy that microdactyly has been found in some cases reported as myositis fibrosa but those who believe that the two conditions are distinct point out that myositis fibrosa is commoner in girls and in older patients, that it more often occurs in the lower limbs and that it is accompanied by pain—even severe pain—much more frequently than is myositis ossificans. Myositis fibrosa is said to attack the muscles of respiration and the laryngeal muscles and to run a more rapid course even to a fatal termination (Mair 1932) The muscles have been described as feeling like a sandbag and the overlying skin may be erysipeloid in appearance

In calcinosis universalis, calcareous deposits may occur in the skin and subcutaneous tissues as well as in muscles and fasciae Radiographically they are seen as granular and fragmentary opacities distinct from the shadows cast by the bony skeleton. The same is true of the opacities seen when dermato-myositis results in calcification. In calcinosis the deposits may be absorbed whereas in myositis ossificans progressiva when bone is once formed it never disappears.

Dermato-myositis affects the extremities and only later the trunk. There may be fever and sweating, and the spleen is enlarged. The diaphragm, intercostal muscles and palate are affected With intermissions the course extends over a period of eighteen to twenty four months, but not longer Nevertheless the two affections, dermato-myositis and myositis ossificans, do seem to be closely related.

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CASE 70—MYOSITIS OSSIFICANS PROGRESSIVA

(Figs. 215 to 219) Female aged seven years. Extra-skeletal ossification first noticed when she was two and a half years old. Had been treated by prolonged recumbency for glands. One of family of eight others normal. On admission—mild kyphotic curve dorsal and lumbar regions of spine completely rigid. Some movement in cervical spine Erector spinae large and hard. Hard column in left latissimus dorsi another mass in the right lumbar region. Bridge of bone in right pectoral muscles with bony protuberance fixed to the sternum. Upper limbs normal but thumbs rather short. Suspicious firmness of left calf (with doubtful shadow in radiograph) Reflexes normal Bilateral equinus. Great toes small and dorsiflexed first metatarso-phalangeal joints prominent bilateral hallux valgus. Radiographs showed ectopic bone in the dorso-lumbar region on both sides, in the left cervico-dorsal muscles and in the right pectoral First metatarsals abnormal proximal phalanges of great toes absent (possibly fused to metatarsals)

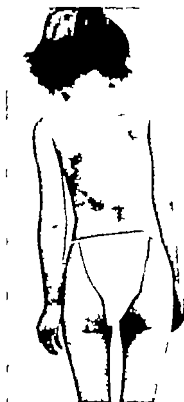


FIG 215

Case 70—Photograph shows sw llmrs nd deformity of the back There is ertical col mn of bone to the left of the mid-line in the cervico-dorsal region

Tendo achillis lengthened on both sides. The opportunity was taken of removing the bar of bone from the right pectoral muscle the mass consisted of a gelatinous lump containing bone and this resulted in definite improvement in the mobility of the limb Report from the mother thirteen years later "She is still deformed the shoulders and spine and the muscles of the right hip are ossified. She can, however walk quite well and she leads a normal life but cannot stoop to put on her shoes. She suffers no pain and is always cheerful and bright. Although the condition has progressed extension of the ectopic ossification appears to have been slow



FIG. 216

Case 70—Radiograph shows ectopic bone in *the left postero-lateral tissues of the neck.*



FIG. 217

Case 70—Microdactyly First metatarsals *appear to be lengthened by fusion* with the proximal phalanges.



FIG. 218

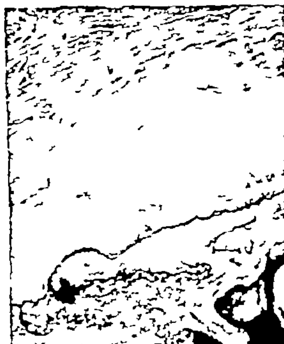


FIG. 219

Case 70 Histological sections of the mass removed from the right pectoral region. Note in Figure 218 the degenerating muscle fibres (left bottom) newly formed bone and cartilage (right top) and intervening fibrous tissue Figure 219 shows dense fibrous tissue merging below into cartilage and bone (× 74)

CASE 71—MYOSITIS OSSIFICANS PROGRESSIVA

(Figs 220 to 224) Male aged sixteen years. No abnormality noticed at birth. At four months a swelling appeared on the scalp this disappeared completely At two years a swelling appeared on the front of the neck aspiration yielded blood only During the next five years similar swellings appeared in various parts of the back. Sometimes they followed trauma and they gave the impression of moving from place to place. Some disappeared completely but others left residual induration and stiffness. The swellings were not painful or tender By the age of seven years the spine was completely rigid and movements of the arms were limited Bone was removed from the right latissimus dorsi without benefit. Further swellings appeared but progress was generally slow except for increasing limitation of movement of the mandible since the age of eleven years. Youngest of family of ten. No other member of family affected with myositis or microdactyly

On admission spine rigid except for some movement in the cervical and upper dorsal regions. Chest expansion one inch. Bony plaques found at back of neck and in the dorsal and lumbar regions, especially in the latissimus dorsi and trapezius, left masseter left sternomastoid (fused to clavicle) and right pronator quadratus. Outgrowths of bone from the lesser trochanters and adductor tubercles of the femora (very similar to exostoses in diaphysial aclasis) Plantar fascia involved. Microdactyly of big toes and thumbs. Deformity of great toes similar to that seen in Case 70 Biochemical examinations of blood revealed nothing of importance (Under the late R C. Elmslie)

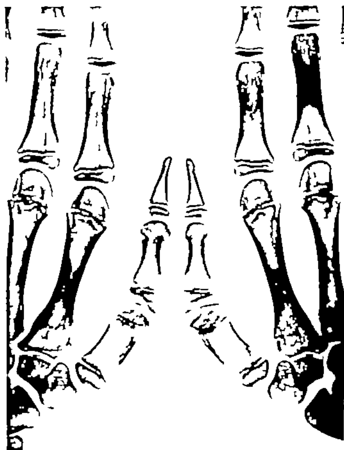


FIG. 220

Case 71—The hand show microdactyly of the thumbs with deformity of the epiphyses of the proximal phalanges



Fig. 221



Fig. 222

Case 71—Figure 221 is a photograph showing the columns and plaques of bone in the back. Radiograph of the dorso-lumbar region shows irregular columns of bone on both sides of the spine (Fig. 222)



Fig. 223



Fig. 224

Case 71—Lateral radiograph of the cervical spine (Fig. 223) shows a branched column of ectopic bone part of which involves the sternomastoid. In Figure 224 it is seen that there is a small but well-defined calcaneal spur

CASE 72—MYOSITIS OSSIFICANS PROGRESSIVA

(Fig 225) Male aged thirty nine years. Details of this patient whose skeleton is preserved in the Hunterian collection of the Royal College of Surgeons of England have been given earlier in this text (page 157) This specimen shows that bone formation is not confined to the muscles nor even to their immediate vicinity

CASE 73—MYOSITIS OSSIFICANS PROGRESSIVA

(Fig 226) Male aged sixty-one years at death. Limitation of head movements were noted in infancy From age of eighteen years disability was serious, and stiffness involved all four limbs. Report on the skeleton of this case in the Museum of Trinity College Dublin, was published by Bennett in the Dublin Journal of Medical Science (1872)

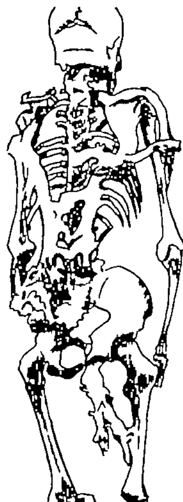


FIG. 225

Case 72—Drawing of skeleton (3794 1) in the Museum of the Royal College of Surgeons of England (after Stonham 1892)



FIG. 226

Case 73—Drawing of skeleton in the Museum of Trinity College, Dublin showing very extensive extra-skeletal ossification (after Stonham 1892)

CRANIO CLEIDO DYSOSTOSIS

This congenital condition is characterised by deficient formation of the clavicles with delayed and imperfect ossification of the cranium associated in many cases with other anatomical errors. The first case of clavicular defect is said to have been reported by Martin (1765) One with both clavicles and the skull affected, was reported in 1871 by Scheuthauer Marie and Sainton (1898) named the condition hereditary cranio-cleido-dysostosis and called attention to irregularities in the dentition For long it was thought that the changes were confined to bones that normally ossify in membrane but in fact, bones preformed in cartilage are often affected.

In view of the widespread and variable abnormalities discovered in cases that might be regarded as belonging to this group Rhinehart (1936) suggested the alternative title of mutational dysostosis—a suggestion that was supported by Soule (1946)—but this seems to be much too comprehensive a title Three valuable reviews of the subject have been published by Fitzwilliams (1910) Fitchet (1929) and Soule (1946)

Hereditary and familial influences—Heredity undoubtedly plays an important part in the incidence Stocks and Barrington (1925) found that the condition was inherited in more than half the cases they collected namely in 96 of a total of 144 It has been traced through five generations (Soule 1946) but it is said as a rule to disappear after two or three generations It may be inherited through either parent with about equal frequency Soule combining Fitchet s figures with his own found that in a total of 323 cases 198 were familial these occurring in fifty-two families, while 125 cases were sporadic.

Sex—Both sexes are affected to an approximately equal extent.

Age—It may be discovered at any age. The cranial deficiencies may be noticed at birth Fitzwilliams cases included a baby one month old and a woman of sixty years. The defective clavicles cause little if any disability and may easily escape notice for many years but nearly 0 per cent of the reported cases were discovered before the age of twenty years.

Etiology—The cause of this primary error of development is entirely unknown. It is one of the conditions that Jansen (1921) attributed to increased intra-uterine pressure but his theory has not been generally accepted. There is no doubt that the development of the clavicles must be disturbed at a very early stage of foetal life It has been discovered in a twin a girl the other twin, a boy being normal.

Distribution of the abnormalities—This shows considerable variation The clavicular error is present almost without exception and is usually accompanied by deficiency of the cranium. Defects in the skull appear to be always symmetrical. As to the clavicles one or both may be defective Fitzwilliams found a unilateral defect in only six of sixty cases. Stocks and Barrington found bilateral defects in 8* per cent of their cases only two patients both with typical changes in the skull had normal clavicles Other sites of developmental errors are the teeth, the mandible the hands and feet the pubis the femoral necks and the neural arches. Paltauf (1912) seems to have been the first to note the gap in the pubic symphysis. Crouzon and Bouttier (1921) suggested that a case with deficient ossification of the pubis be labelled *forme cleido-crânio-pelvienne* while Latham (1945) proposed the term cranio-pubo-dysostosis for a case with normal clavicles.

Clinical signs—The striking features of a typical case are the slender build the large head with small shrunken face long neck drooping shoulders and narrow chest *Growth of the* whole skeleton is retarded and there may be a certain degree of dwarfism but this is not a

marked feature as a rule. The mentality is normal In at least one-third of the cases the skull shows well-marked frontal prominences separated by a median gutter The parietal bones and sometimes the occipital bone may also form prominences making six bosses in all on the skull (Stocks and Barrington 1925) The orbital ridges are well marked but the lower margins of the orbits are shrunken or even deficient. The anterior fontanelle is large and may never close completely In some of the younger patients a much greater deficiency in the calvarium is seen. The eyes are rather far apart. The palate is high. A mild degree of hydrocephalus may be present. The maxillae are small so that the relatively large mandible may be prognathous. Delayed eruption, non-eruption and incomplete development of the permanent teeth are common. The temporary teeth erupt well and may be retained longer than normal but when they are shed the non-eruption of permanent teeth may necessitate the wearing of dentures. Supernumerary permanent teeth are sometimes present Dentigerous cysts may occur

As a rule the defects in the clavicles are easily felt Sometimes there is no more than a kink in the middle of the bone or merely a dimple of the skin. The position of the shoulders —low and a little forward—and their abnormal mobility are no more than would be expected. Though the muscles may be defective in some anatomical details their power is not usually diminished Many patients reach adult life entirely unaware of the defect in spite of hard manual work involving heavy lifting Noticeable weakness of the shoulders and a tendency to undue fatigue are exceptional. When both clavicles are affected the shoulders can be approximated voluntarily in front of the chest to an abnormal degree and can be made to meet by gentle passive force The scapulae may be small somewhat deformed, rather winged and prominent and more mobile than normal. Subluxation of the humeral head has been found in a few cases. The dislocation was complete in one case (Gross 1903) and could be easily completed by manipulation in another We found both humeral heads subluxated downwards in a boy aged seven years. Bilateral subluxation of the radial heads has also been reported. Unusual length of the first finger is not uncommon. The fifth metacarpal may be shorter than normal. The terminal phalanges and the nails are short particularly in the thumbs and great toes.

Other skeletal abnormalities have been found in individual cases. Postural defects and spinal curvature are common. Spina bifida occulta often widespread in the spine is of no clinical importance Syringomyelia has been found as a complication. Widening of the symphysis pubis and deficient ossification of the pubic bones are not obvious clinically and even when sought are often not palpable. In younger patients the pubes are present though partly or completely devoid of ossification. Coxa vara can be recognised by the usual signs. Other deformities that have been reported in individual cases are subluxation of a hip or a finger joint and absence of the radius. In a case with deficiency of only one clavicle there was bilateral synostosis of the radius and ulna (Avery 1930)

Radiographic appearances—*Skull*—The membranous calvarium shows various degrees of imperfect ossification The base is ossified normally The sutures often fail to close normally The anterior fontanelle is large and may never close it may reach nearly to the level of the orbital ridges even in an adult Occasionally there is a larger defect anteriorly even in middle life A fontanelle may be present posteriorly in both mastoid regions and also in the sphenoid. The mastoid itself may not be pneumatised (Salmon 1944) Wormian bones are seen in the occipital and posterior parietal regions. The frontal sinuses are often absent but occasionally they are disproportionately large, the other sinuses being small. In extreme cases there may be no ossification whatever in most of the vault. In one of our patients, aged three years, the two parietals were apparently unossified. The pituitary fossa may be small but it shows no constant change The maxillae are hypoplastic but the mandible is of normal dimensions fusion at the mandibular symphysis may be delayed or even fail to occur There was no sign of fusion in a boy aged eight years reported by Ingham (1947) The mental tubercles

may be unusually long. The nasal lachrymal and malar bones may be incomplete or absent (Salmon 1944). In some cases ossification of the skull is normal.

Clavicles—Stocks and Barrington (1925) found that the commonest defect was absence of the outer end of the clavicle the sternal half being present. The next commonest condition was the presence of two separate fragments for each clavicle (28.2 per cent —but this figure seems unduly low). The inner fragment was usually the larger of the two the outer may not reach the acromion. The least common defect was absence of the sternal end with the acromial end present. Complete absence of both clavicles was uncommon (8.1 per cent) and absence of one clavicle only was exceptional. These findings are supported, more or less by other authors. Stocks and Barrington found pseudarthrosis between the two fragments in only three cases the adjacent ends of the fragments in such cases may be enlarged or they may overlap. In only two of their cases both with typical skull changes were the clavicles normal. Nettesheim (1926) reported the case of a woman aged twenty-nine years with the left clavicle in three pieces and the right in two. Everley Jones (1937) rightly called attention to the need for care in examining radiographs since a clavicular fragment may easily be overlooked. In ten cases with clavicular defects this author found both clavicles represented by two fragments in all but one in this there were two clavicular fragments on one side and only the sternal portion present on the other. The bones of the *limbs* generally are rather slender. In many of the recorded cases it seems probable that the pelvis and hips were not specially examined so that the frequency of abnormalities in this region is uncertain.

Pubes—In most cases no reference is made to the condition of the pubes. In the author's small series of eleven cases ten, varying in age from three to eighteen years showed deficient ossification of the pubis, the deficiency being bilateral in all. In the other case—an adult woman—the pubes were well ossified but her two affected children both showed defects of the pubes as well as other signs of dysostosis. The degree of deficiency was found to vary. In three patients there was complete absence of ossification in the pubes both body and rami. The oldest patient of this group was a boy aged fifteen years who showed some stippling in the pubic part of the acetabulum. In six of the remaining seven cases there was a fragment of bone of varying size in the horizontal ramus, the body and descending ramus being completely unossified. Ossification of the pubis is only delayed it occurs eventually though often incompletely. The inferior ramus of the ischium shares in the delayed and defective ossification. The symphysis may remain unusually wide with an irregular boundary on each side. In such cases the fusion of the conjoint rami may be incomplete and their thickness considerably reduced. The case of a woman aged twenty four years with these changes in the pelvis and gross deficiencies in the clavicles was reported by Steel and Whitaker (1937). Imperfect or delayed ossification of the pubes is not however invariably found in cases showing other clear signs of the condition. For instance Fitchet (1929) published six cases in three generations of a family in all of which the pubes were normal and there was no coxa vara. The pelvic ring may be reduced in size but seldom to a sufficient degree to cause trouble in childbirth. The sacro-iliac joints may be increased in width.

Coxa vara—In the author's series of eleven cases there was coxa vara in five—bilateral in three unilateral in two. Both clavicles were deficient in four of these patients the fifth had unilateral coxa vara and a defect of one clavicle both on the same side of the body while failure of ossification of the pubis was present on both sides. The type of coxa vara seems to vary. Klar (1906) the first to record this deformity called the coxa vara in his case congenital. But Ollerenshaw (1938) considered this type unusual. In his opinion the deformity occurred in the upper part of the femoral shaft and he had not seen coxa vara of the infantile type in the "many well marked cases" of cranio-cleido-dysostosis he had seen. The author's experience differs from this for in every case with coxa vara (a total of eight abnormal hips) the deformity was invariably of the infantile or cervical variety (Fairbank [illegible]). Soule (1940) said that infantile coxa vara was common. In Crouzon and

Bouttier's case (1921) the acetabula were deformed and the mobility of the hip joints was much increased.

Spine—Failure of union of the neural arches is common and may involve several vertebrae in the dorsal and lumbar regions. In one case we found spina bifida occulta from the sixth cervical to the sixth dorsal vertebra. In younger patients the vertebral bodies are inclined to be biconvex and the discs biconcave in older patients they may show some reduction in depth Various other congenital deformities of the spine including half vertebrae and incomplete or complete absence of the lower part of the sacrum and coccyx have been reported but such exceptional findings are of little interest and of no diagnostic significance Eltorm (194) reported a curious case a woman aged fifty two years with the dorsal bodies wedged *posteriorly* and showing defective ossification. The ribs may slope downwards to a greater degree than usual. The sternum may be of peculiar shape failure of the manubrium to ossify has been recorded.

Hands and feet—In the hands and feet various abnormalities have been found, the most constant and curious being the presence of epiphyses at both ends of the metacarpals and metatarsals particularly of the second and fifth, and an abnormally long second metacarpal. The epiphysis which occurs at the base of the second metacarpal is strikingly large The ungual tuberosities are poorly developed or absent the terminal phalanges being short and pointed particularly in the thumb and great toe (Brailsford 1935) The intermediate phalanges may be small they may show curious ossification or even be absent. Ossification of the carpus may be delayed. The calcaneum may be short.

Complications—Pressure on the brachial plexus relieved by removal of the outer fragment of the clavicle was reported by Poynton and Davies (1914) One patient who complained of pain and numbness in the ulnar area accompanied by cyanosis, was treated by bone-grafting operations on both clavicles (Everley Jones 1937) Ollerenshaw (1938) reported two cases a brother and sister with calcification in the skin and soft tissues. Syringomyelia has been mentioned already as a rare complication.

Pathology—There is no abnormality in the bone of the calvarium and clavicles except the limitation of its distribution. The base of the skull is said to be narrowed, especially in the middle portion. The cranial bones are thickened where bosses occur The muscles acting on the shoulder girdle show a number of abnormalities varying with the type of clavicular deficiency (Fitzwilliams 1910 Everley Jones 1937) Their relative frequency corresponds broadly with that of the various deficiencies of the clavicle The commonest are absence of the clavicular portion of the trapezius and the anterior fibres of the deltoid. Occasionally the sterno-mastoid and pectoralis major are deficient but the clavicular parts of these muscles are affected only when the sternal part of the clavicle is very small or completely absent—a rare occurrence When the sternal portion alone is present the bone is prolonged outwards by a ligament or fibrous band which in most cases passes to the coracoid and not to the acromion The ligament may even be attached to the glenoid or to a rib (Fitzwilliams) it is regarded as the costo-coracoid membrane When there are two fragments these are usually united by a ligament

Diagnosis—This should present no difficulty Absence of ossification of the pubis may be of diagnostic value If found by accident it may lead to the discovery of deficiencies in the skull and clavicles. In a young patient showing pseu[illegible] clavicle with thickening of the fragment and without [illegible] deficiency in the [illegible]graphic examination of the pelvis might remove any [illegible] the case be [illegible] error of development and not to trauma. Evans (19[illegible] [illegible]d the case of [illegible] an absent tibia and complete absence of ossific[illegible] [illegible]ral head on [illegible]le and in the pubes on both sides. The condition of [illegible] not menti[illegible] [illegible]ars to have been normal

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CASE 74

CRANIO-CLEIDO-DYSOSTOSIS

(Fig 227) Tracing of the radiograph published by Steel and Whitaker showing the wide symphysis and imperfect ossification of the pubes and conjoint rami in a woman of twenty four years. There were deficiencies in the skull and absence of the outer two-thirds of both clavicles.

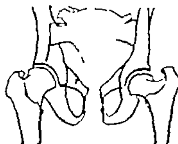


FIG 227

CASE 75—CRANIO-CLEIDO-DYSOSTOSIS

(Figs. 228 to 234.) *Male aged seven years. One of a family of seven children the others being* normal. Has always presented the same general appearance with large head and narrow shoulders. Typical changes in the skull, clavicles, pubes, hands and feet Anterior and temporo-parietal fontanelles patent and membranous frontal and parietal eminences prominent. Marked frontal fissure No sign of frontal sinuses which should be visible at this age Wormian bones in the occipital region. Lambdoid suture closed. Teeth very irregular On extraction of carious temporary teeth there was practically no absorption of the roots. The shoulders can be " bunched together " The right shoulder droops more than the left radiographs showed that the humeral head was subluxated downwards.

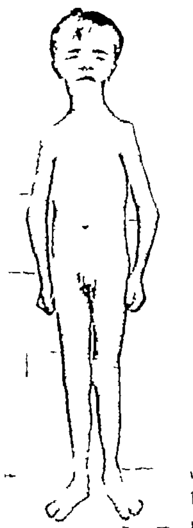


Fig 228

Case 75—Large head small face arrow shoulders and chest, slender build generally Not that the head of the right humerus is low than the left



Fig. 229

Case 75—Posterior view — small and markedly winged scapulae.



Fig 230

Case 75—A tero-posterior radiograph of the skull showing the large anterior fontanelle Th metopic suture is widely open in its pper two-thirds.



Fig. 231
Case 75—Chest and shoulders showing th narrow thorax. The right clavicle is represented by two fragments and the left cla icle is deficient in its outer part where it fails to reach the acromion.



Fig. 232
Case 75—Hand showing delayed ossification of the carpus, epiph ses at the bases of the second and fifth metacarpals, nd abnormal shape of the interm d at d t rminal phalanges.



Fig. 233
Case 75—Feet showing additional epiphyses at the bases of the second metatarsals. The shape of the internal cuneiforms and of the phalanges, particularly of the great toes, is abnormal.



FIG. 234

Case 75—Pelvis and hips showing absence of ossification in the bodies and descending rami of the pubes, and delayed ossification in the inferior rami of the ischia. The horizontal pubic rami are represented by oval fragments of bone.

CASE 76—CRANIO-CLEIDO-DYSOSTOSIS

(Fig 235) Female with bilateral clavicular dysostosis each clavicle being represented by two fragments. Skull apparently normal (but not radiographed) Pubes ossified but distinctly less dense than the rest of the pelvis. No coxa vara. The width of the symphysis is approximately normal. The patient had three children two affected by dysostosis both had bilateral clavicular dysostosis all four clavicles being in two fragments. In the elder child, a boy aged twelve years, there was no ossification of the pubic body or descending ramus on either side whereas the horizontal rami consisted of bone there was coxa vara on the right side only the only abnormalities in the skull were absence of the frontal sinuses and presence of Wormian bones in the occipital bone. The younger child a girl, showed similar bilateral delayed ossification of the pubis but no coxa vara.



FIG. 235

Case 76—Each clavicle is represented by two fragments. Note that the outer fragments do not reach the acromia. On the left side the two clavicular fragments overlap

ASE 77—CRANIO-CLEIDO-DYSOSTOSIS

Figs. 236 and 237) Female aged six years. Always weak on legs gait waddling Lordosis resent Skull generally well ossified. Wormian bones in the occipital region. Bilateral ivision of the clavicle into two fragments. Bilateral coxa vara, which radiographs showed o be of the cervical or infantile type. Subtrochanteric osteotomy performed on both femora he body and descending ramus of the pubis and the ascending or inferior ramus of the chium are unossified on both sides. The horizontal rami of the pubes are ossified. On alpation no deficiency can be felt in the pubic region. Additional epiphyses and other hanges present in the hands. The terminal phalanges of the toes particularly of the great oe are typical.



FIG. 236

Case 77—Thorax and shoulders showing both clavicles in two fragments, the outer being smaller and not making contact with the acromion.



FIG. 237

Case 77—Pelvis and hips showing absence of ossification in the bodies of the pubes and the conjoint rami, and typical infantile coxa vara of both femora. Note that the horizontal rami of the pubes are ossified

CASE 78—CRANIO-CLEIDO-DYSOSTOSIS

(Figs. 238 to 241.) Male aged three years. No abnormality noticed by the parents. Fourth of four children, the others and the parents being normal. Gross deficiency in the calvarium: the parietals show little if any signs of ossification: anterior fontanelle very large. Two fragments for each clavicle. Epiphyses at both ends of all metacarpals. Ossification of carpus delayed. Both pubes completely devoid of bone. No coxa vara. Delayed fusion of mandibular symphysis and of neural arches of the spine. The density of most bones is below normal. (Under Sir L. Barrington Ward.)



FIG. 238



FIG. 239

Case 78—Skull showing enormous fontanelle limited union of the two halves of the frontal bone and absence of fusion at the mandibular symphysis (Fig. 238). In the lateral view note the gross deficiency in ossification particularly of the parietals, and many Wormian bones in the occipital (Fig. 239).



FIG. 240



FIG. 241

Case 78—Pelvis showing complete absence of ossification in the pubes and inferior rami of the ischia (Fig. 240). The lower forearm and hand (Fig. 241) shows osteoporosis of the bones, double epiphyses for all metacarpals, and a curious shape of many phalanges.

CHAPTER 16

NEUROFIBROMATOSIS

This is a congenital affection characterised by pigmented spots on the skin cutaneous fibromata multiple neurofibromata of the cranial and peripheral nerves, and in some cases, skeletal changes, endocrine syndromes and heterogeneous tumour formation of the nervous system. According to Kinnier Wilson (1940) it was first described by R. W. Smith in 1849 In 1882 the histology was discussed by von Recklinghausen whose name is still attached to the disease by many Valuable accounts of the skeletal changes were published by Brooks and Lehman (1924) and Holt and Wright (1948) and in children by Leader and Grand (1932) In tuberous sclerosis a rare condition possibly allied to neurofibromatosis (Weber 1924) bone lesions have also been described (Heublein *et al* 1940 and Ackermann 1944)

Hereditary and familial influences are in evidence not uncommonly It has been seen in six generations (Gardner and Turner 1940) Four brothers showing signs of the condition were reported by Garland (1941)

Age—It is seen at all ages. Since at least some skin lesions are present at birth the condition may be recognised within the first few months of life. In some cases there appears to be an exacerbation at puberty

Sex—Males are rather more frequently affected than females.

Etiology—It is considered to be a congenital anomaly due to defective germ plasm, but the cause is entirely unknown. Trotter (1926) suggested that faulty insulation of nerve fibres was responsible

Clinical signs—In most cases typical lesions in the skin are present and the diagnosis is obvious. The skin lesions are of two kinds, café au-lait spots or freckles and fibromata. The pigmented spots have smooth outlines and vary in size from a pin head to a five-shilling piece but occasionally they are much larger They tend to increase in size and number as the child grows. The distribution varies, but in some cases this is limited to the region of the pelvis and adjacent parts of the trunk and thighs. The cutaneous fibromata (fibroma molluscum) are either flat or raised. The colour may be that of the surrounding skin or it may be pink violet or blue. They are of all shapes and sizes from a millet seed to an orange. Some present as a fold others are pedunculated. They are soft and may feel like a bag of worms. There may be thousands present covering the entire body Usually they are symptomless. The fibromata of nerve trunks may be in, on or loosely attached to the nerves. They may be confluent. Those that are subcutaneous or reasonably accessible can be readily felt They may be painful or tender even sufficiently tender to produce protective spasm. There may be a plexiform neuroma pachydermatocele or elephantiasis of a limb in each of these conditions a bone in the vicinity not uncommonly shows radiographic changes. The nervous syndromes met with naturally vary with the locality of the fibromata. Tumours of cranial and spinal nerves or of the cord or brain give rise to a variety of symptoms even to a sensori-motor paraplegia.

As in other conditions the syndrome may be incomplete the lesions being confined to the skin or to the nerves or they may be entirely central.

The skeletal affections are of two kinds—scoliosis and changes in the bones. Scoliosis is by far the commoner occurring in about half of the cases. The part most commonly affected primarily is the lower dorsal region but it may begin in the cervical. It is often associated

with some kyphosis and is definitely progressive. Pain may be a troublesome feature. In advanced cases the rotation of the vertebrae is marked and the curves are very abrupt. Paraplegia has actually resulted from the severity of the deformity alone (Miller 1936).

Changes in the bones, said to occur in 7 per cent. of the cases (Reuben 1934), are usually free from symptoms. Skin and bone lesions may be superimposed. They may be associated with either diminution or accentuation of growth of a bone; the latter is more common and is rarely seen without soft tissue changes in the neighbourhood. Only exceptionally do changes in the bone lead to a fracture and pseudarthrosis. Bowing of a tibia may precede pseudarthrosis and the bowing may even be present at birth (Holt and Wright 1948). General asymmetry of the face, body and limbs with unilateral distribution of the bone changes was described by Friedman (1944). Cases with neurofibromata affecting the viscera have been described.

Blood examination gives negative results.

Radiological appearances—In most cases the scoliosis is unaccompanied by obvious lesions in the vertebrae. There may, however, be "cystic" changes in the bones (Capener 1935, Seddon 1935). Collapse of a body may occur. Erosion of the bodies from behind or enlargement of the intervertebral foramina may result from pressure by neurofibromata of spinal nerves. In a case published by Pugh (1930) there was an open clear wedge in the mid-dorsal region on the convex side of the curve, suggesting that an intervertebral space had gaped.

In other parts of the skeleton a variety of changes may be seen. A periosteal neurofibroma may cause smooth erosion of the cortex; in such a case a thin shell of bone is occasionally formed by the periosteum over the fibroma, the appearance being that of a cortical "cyst." The bone adjacent to a cortical erosion usually shows increased density which may be widespread. There may be "cystic" lesions *in* a long bone, but some which are apparently endosteal are really cortical in origin. A case with a large smooth excavation in the left ilium and complete disappearance of the horizontal ramus of the right pubis was reported by Heublein *et al.* (1940). Curious multiple cystic changes in the metaphyses of several of the long bones (the appearance being a little suggestive of dyschondroplasia), with the mandible and one vertebra also involved, were reported in an infant by Holt and Wright (1948). In another case published by these authors (a girl of four months) with less marked changes, the bone lesions disappeared completely. Increased density of the shaft of a bone may occur with no obvious erosion of the surface by an adjacent fibroma; this increased density often ends in streaks towards one end of a bone. Occasionally irregular thickening of a bone is seen. As already stated, an affected bone may be shorter or longer than its fellow. Tanner (1946) reported a case with a large neurofibromatous tumour adherent to the bones on the front of the leg, and with the tibia (but not the fibula) four and a half centimetres longer than the other and showing extensive irregular sclerotic changes in a radiograph. A somewhat similar case with the periosteum over the tibia greatly thickened was reported by Weber and Perdrau (1930). The ribs and the mandible sometimes show changes. An osteomalacic condition, particularly affecting the ribs, has been reported by Gould (1918), and multiple incomplete fractures by Brailsford (1948).

Associated with elephantiasis two types of osseous change may be found affecting one or more of the bones—increase in both density and length and diminution of calibre without other structural change. Brooks and Lehman (1924) reported a case in which one tibia was eight centimetres longer than its fellow. In a case reported by Friedman (1944), a man aged thirty-one years with elephantiasis of one leg below the knee, there were several smooth indentations on the anterior surface of the tibia and considerable dense thickening of the bone; the affected leg was three centimetres longer than the other. The shafts of the humerus, radius and ulna were curiously slender in an arm affected by elephantiasis in one patient, and long thin metatarsals were seen in the foot of another; after amputation of this foot the fibula became attenuated (Holt and Wright 1948). In a third case published by these authors

similar changes were found in a clavicle and some ribs after removal of a supraclavicular neurofibroma. Slender bones may however occur without obvious changes in the soft tissues. A long thin humerus, associated with clear bulbous ends to each of the three bones forming the elbow joint which was dislocated, was noted by Mondor and Leger (1946) In one case we found curious sharp lipping of the margins of the great trochanters and the ilia, a feature we have not seen reported by others (Fairbank 1939) The skull may show patches of either increased or decreased thickness but these are exceptional Increased density suggestive of leontiasis but without thickening we found in one case. Erosion of the occipital and petrous bones associated with a tumour of the auditory nerve was reported by Camp (1920) The pituitary fossa may be enlarged but as a rule it is normal.

Progress—The various types of lesion skeletal and other may or may not be progressive. The scoliosis, however usually shows a tendency towards progressive increase of the curves in spite of careful conservative treatment and may eventually cause severe or complete crippling—an important fact to keep in mind when treatment is under consideration.

Complications—Paraplegia may develop in cases with severe scoliosis, even in childhood as already mentioned it may also result when fibromata develop on spinal nerves. Complications arising from endocrine errors include acromegaly—three such cases were reported by Tucker (1944)—and hyperparathyroidism. It has been suggested that occasionally the two conditions described by von Recklinghausen neurofibromatosis and hyperparathyroidism are associated (Stalmann 1933 Cohen and Doudy 1936) Sarcoma undoubtedly develops in some cases, but the frequency is uncertain 12 per cent. is the figure given by Hosoi (1931) and 6·5 per cent. by Holt and Wright (1948) Neurofibromatous tissue was found in a tibia adjacent to a definite sarcoma of the bone (Norley *et al* 1945) Sarcomatous change may occur in more than one fibroma (Miller 1936) Neurofibromatosis Paget's disease and sarcoma of the pelvis were associated in one case known to us a man of fifty three years.

Mental deficiency and syringomyelia have been reported in association with neurofibromatosis.

Pathology—The neurofibromata consist of reticular connective tissue with a few nerve fibres—myelinate or amyelinate—winding about either singly or in thin bundles. In places are seen cells with long hair-like tails, arranged in sheaves or palisades and proved by stains to be collagenous and fibro-glial Hyaline degeneration of the connective tissues precedes jelly like deposits—the cyst-like lesions—into which haemorrhage may occur (Kinnier Wilson 1940) In plexiform neuromata and elephantiasis there is loose connective tissue containing nerve strands fantastically overgrown. The skin tumours are practically pure fibromata only a small proportion include nerve fibres.

As to the bone lesions, the neurogenic origin of those which are subperiosteal is readily acceptable but this is not so with those which are endosteal. Nevertheless the typical fibrosis with whorls of cells has been found in some lesions apparently endosteal. Uhlman and Grossman (1940) found whorls both in a soft tissue tumour and in the underlying cystic jaw of a girl of sixteen years. An intra-osseous neurofibroma was found at the site of a spontaneous fracture of the tibia in a girl of seven years (Green and Rudo 1943) and, as already referred to in a leg amputated for sarcoma (Norley *et al* 1945) Neurofibromatous tissue may or may not be found at the site of a pseudarthrosis.

We have discovered no clear statement as to the nature of the pathological changes in a bone showing diffuse increased density with neither cyst formation nor erosion of the cortex by a subperiosteal neurofibroma Tanner (1940) considers that sclerosis is a late development and follows earlier rarefaction and softening Collagenous and myxomatous degeneration in osseous lesions with formation of cysts containing brownish fluid (the result of haemorrhage) are mentioned by Thannhauser (1944)

The cause of the scoliosis where there is no cystic or other lesion in a vertebral body is

obscure There is usually no definite evidence of paralysis but this may occur when a spinal root is the seat of a neurofibroma. Eden (1941) reported a case with multiple dumb-bell tumours of the posterior roots. In ordinary cases he likens the scoliosis to that seen in syringomyelia. It has been suggested that the deformity is due to derangement of tonic nervous control of the vertebral muscles.

Diagnosis—This should present little difficulty The cutaneous nodules and subcutaneous neurofibromata should distinguish neurofibromatosis from polyostotic fibrous dysplasia with areas of pigmentation. These areas are smooth and generally much larger than the café-au-lait spots of neurofibromatosis. The bone changes may be somewhat similar

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CASE 79—NEUROFIBROMATOSIS

(Figs _4? to 44) Female aged twenty-one years. Complained of shooting pains from the little toe up the back of the right leg to the hip for the previous ten weeks. Pain not affected by exercise or rest. Swelling at back of right thigh as long as she could remember painless until present attack. Pigmented areas of skin present since birth. Family history negative. On examination—dark-skinned woman. Pigmentation on outer side of right ankle back of

leg whole of thigh, and both buttocks extending forwards on to abdomen. On the pigmented area of thigh there were circular black spots. Hairy mole on left buttock. Pigmented spots on chest and arms and pigmented patch on left ankle. Pain confined to pigmented area of right leg. Swelling on back of right thigh felt like a loose bag of skin partially filled with fat containing hard round masses. Liver slightly enlarged. Diminished sensibility to pinprick in the area corresponding to the pain. Mild scoliosis. Temperature swinging to 100 degrees. Radiographs showed increased density of the shafts of the major long bones of the right leg especially the femur in which the density ends below in streaks. A cortical indentation is seen on the inner side of the upper third of the shaft of this femur possibly the site of a periosteal neurofibroma. The lumbar vertebral bodies are relatively deep and the transverse processes more slender than usual. (Under the late Dr Douglas Firth.)



Fig. 242



Fig. 243



Fig. 244

Case 79. Figure 242—Pelvis and hips, showing the slender pubic and ischial rami, sharp lipping of the lower margin of the right anterior superior iliac spine and of the margins of the great trochanters. Note the narrow joint space of the right hip, the exuberant rounded lipping on the femoral head and also on the lesser trochanter. Figure 243—Right femur and knee joint, showing distortion of the posterior surface of the shaft and increased density ending below in streaks. Note indentation of the cortex on the inner side of the upper third of the femoral shaft, and suggestion of abnormal density in the tibia. Figure 244—Lumbar spine showing the vertebral bodies relatively deep and the transverse processes more slender and specular than usual.

CHAPTER 17

ARACHNODACTYLY

Synonyms—Marfan's Syndrome, Spider Fingers

This is a rare congenital condition characterised by long hands and feet, and general muscular weakness. It was first described by Marfan (1896) under the title of dolichostenomélie but Achard (1902) suggested the name arachnodactyly by which it is generally known to-day. Weve (1931) considered Congenital Mesodermal Dystrophy a better title but this has received little support. Though undoubtedly a rare condition, it is highly probable it is not as uncommon in this country as the number of reported cases suggests. A friend, Dr H. M. Churchill, supplied the author with details of four cases seen within a few months in the clinics of one county and of a fifth case living in an adjacent county. A useful review of the condition was published by Young (1930).

Hereditary and familial influences—Hereditary influences occasionally play a part in the incidence and it is certainly familial in some cases. The percentage of cases in which these influences are in evidence appears to be rising, no doubt as a result of more careful inquiry before publication of new cases. Not all the members of an affected family show signs of the condition.

Sex—Both sexes are affected to an approximately equal extent.

Age—It is usually obvious at birth and only rarely has it appeared to develop a few years later. Cases have been reported from a month or two after birth up to adult life but the majority have been under ten years of age.

Etiology—The cause is entirely unknown. Various suggestions have been made, particularly endocrine errors, but with little foundation. A pituitary fault seems to be excluded by the fact that while there is an overgrowth in length of the bones they are disproportionately slender. A mesoblastic defect is insisted upon by some but without diminishing our ignorance as to the cause. If not identical it seems to be closely allied to amyotonia congenita as many authors have pointed out. Passow (1933) regarded it as allied to a mild form of syringomyelia—status dysraphicus.

Clinical signs—The typical case is rather above the average in height for his age, of slender build with poorly developed muscles and little subcutaneous fat. The head is long, dolicho-cephalic and the facies rather anxious or old for the age. The supra-obrital ridges are prominent. The ears are large and often irregular in shape, the concha being deep and wide. The palate is high. Mentally the cases are up to the average. The chest is poor, being funnel-shaped or flat with the sternum depressed. Kyphosis with or without scoliosis, the natural result of the muscular weakness, is common, the deformity is purely postural in most cases and readily correctible by suspension. The *limbs* are disproportionately long, the excess becoming more marked from the shoulder and hip downwards, the forearms are more affected than the upper arms and the hands and feet show the greatest amount of lengthening. The disproportion in length of the arms in one case was so marked that the fingers reached the heads of the fibulae. The excessive length of the fingers—"*spider fingers*"—and the total length of the feet are particularly striking and usually suggest the correct diagnosis. *Hypermobility* is common in the wrists, ankles and digits and is seen occasionally in the major joints, the hips, knees and elbows, with the result that the limbs can be placed in grotesque positions. On the other hand *contractures* may occur with limited extension of some of the major joints, *e.g.* the elbows and knees, while in the same cases the more distal joints are abnormally lax. Joint laxity appears to be three times as common as contracture. The excessive mobility of the thumb is a striking feature in some cases. Webbing of the digits has been reported. "Spurring" of the heel, the os calcis being unduly long, is seen in many cases but not in all. Calcaneus or other deformities of the feet may be present. In a

case seen with Professor Alan Moncrieff a girl of twelve years, the big toes were unduly long and large Similar overgrowth of the big toes was seen in another rather less definite case of arachnodactyly a boy of two and a half Brailsford (1044) mentions that a case with hypertrophied big toes was reported by Albanese (1031) Traub (1030) published a case of Epiphysial Necrosis in Pituitary Gigantism, a boy of six years with large big toes and arachnodactyly of the hands and feet An important feature is the general *hypotonia of the muscles* to which attention was first directed by Thursfield (1020) Apparently this muscular weakness is not progressive The electrical reactions of the muscles may be somewhat diminished but are otherwise normal Two of Dr Churchill s cases aged four and five years respectively were so feeble they were unable to stand. The weight is low and the general resistance to infection is diminished. Few cases reach maturity but of these some live to old age Bilateral habitual dislocation of the shoulder and radio-ulnar dislocation have been reported. The ligamentum patellae was elongated in at least two of the reported cases the father of one of them having the same anomaly combined with arachnodactyly (Ormond 1024 and 1030)

The eyes are abnormal in about 50 per cent. of the cases, and in about half of these there is congenital dislocation of the lens. It is said the error in development of the eyes in such cases must have arisen as early as the third or fourth month of foetal life. Tremulous irides and small myotic pupils that do not react normally if at all to atropine have frequently been reported. Strabismus may occur Congenital cataract was reported in one case but was not met with at all in the twenty-six cases reviewed by Young (1000)

Congenital *heart disease* is found in about one third of the cases. Cyanosis of the extremities was present in two of the three cases reported by Wyckoff (1039)

Arachnodactyly was associated with osteogenesis imperfecta and blue sclerotics in three cases (Ellis 1040)

Blood examination has revealed nothing of interest

Radiological appearances—The limb bones are unduly long and disproportionately slender The greatest amount of elongation is seen in the metacarpals and metatarsals and particularly in the phalanges. Extra epiphyses have been seen in some of the metacarpals and phalanges. Epiphysial development was found to be advanced in two cases recorded by Parker and Hare (194) The pituitary fossa is of normal size

Progress—It has been emphasized by several authors that the general muscular weakness is not progressive As already mentioned the poor physique and lowered resistence often result in death from intercurrent disease in adolescence or early adult life

Diagnosis—The disproportionate length of the more distal portions of the limbs and the slenderness of the bones distinguishes it from hyperpituitary gigantism.

The closely allied condition of amyotonia congenita is distinguished by the absence of spider fingers and long feet

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CASE 80—ARACHNODACTYLY

(Figs. 243 to 247.) D. J., male, aged eight years. Two brothers and a sister and his parents normal. Walked at two and a half years. Cannot quite dress himself on account of lack of strength in fingers. Weight 43 lb. 1 oz. Height 4 feet 0 inches. Can run slowly. Gets exhausted easily. Crawls a good deal. Complains of pain in knees or a hip after walking far. Congenital heart disease. Face asymmetrical. Very thin; hardly any muscles. Looks older than his age. Tremulous irides and subluxation of lenses. General ability below average on account of long absences from school owing to ear trouble. Hypermobility of wrists and fingers. No contractures of major joints. Hands and feet long at birth, but latter were not then deformed. Now has calcaneo-cavus of both feet. Is not getting weaker; becoming stronger if anything. Mild scoliosis. (Under Mr. K. I. Nissen.)

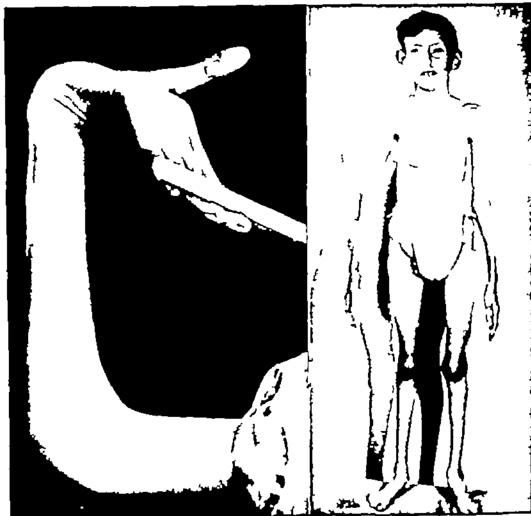


FIG. 245 FIG. 246

CASE 80. Figure 245—Forearm and hand showing hypermobility of the wrist and fingers. Note the length of the fingers. Figure 246—Photo to show the long lanky figure, long hands and feet and poor muscles.



Fig. 247

Case 80—Feet showing excessive length and, in the left foot, the calcaneo-cavus deformity can be seen.

CASE 81—ARACHNODACTYLY

(Fig 248) G H., female aged five years. Sent to hospital for multiple deformities. Typical long hands and feet. Marked deformity of chest Severe kyphosis of whole spine which largely disappears on suspension Calcaneus of both feet Strabismus present. (Under Dr H M. Churchill.)

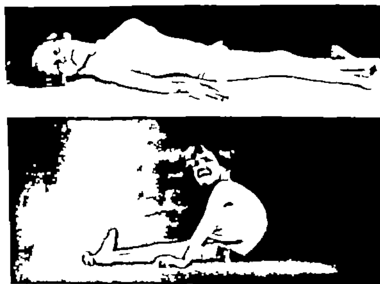


Fig. 248

Case 81 Photos showing the slim build, strabismus, deformity of chest, marked tot l k phosis on sitting, long fingers and feet and the calcaneo deformity of the left foot.

CHAPTER 18

ACROCEPHALO-SYNDACTYLY

This is an uncommon condition in which maldevelopment of the skull is associated with bilateral malformation of the hands and feet and in some cases contracture of one or more of the major joints. It was originally described and named by Apert (1906) An excellent discussion of twenty-nine collected cases was published by Park and Powers (1920) and monographs on this condition have been written by Viallefort (1934) and Ferriman (1941) In about a third of the cases it is familial (Ellis 1948) It may be inherited but not to the third generation (Cohn 1943) The *cause* is unknown, but it must be operative in early foetal life. The deformity of the head is known by various names—acrocephaly oxycephaly tower-skull etc. It is the result of premature synostosis (cranio-stenosis) of the coronal and other sutures of the skull, which leads to raised intracranial pressure exophthalmos (occasionally to an extreme degree) perhaps divergent strabismus, and optic atrophy The precise deformity depends on which sutures have fused. The facial bones are also affected by the synostosis. The palate is high sometimes to a surprising degree Mental deficiency is exceptional. Hypertelorism may be present but this also is exceptional.

Cranio-facial dysostosis of Crouzon and acrocephaly are now regarded by many pediatricians as fundamentally the same condition.

In the extremities may be found a variety of malformations and these are usually symmetrical. Webbing of the fingers is common this may be limited to two of the digits or involve all five—the so-called mitten-hand and sock foot. In addition, deficiencies and malformations of the bones of the hands and feet, of various types may be present. Synostosis of the radius and ulna, and bilateral absence of the radius associated with malformations of the skull have been described

Limitation of movement, even amounting to ankylosis of one or more of the major joints particularly the elbow may occur either with or without syndactyly The shoulders hips and knees are sometimes affected. As is well known acrocephaly may occur without deformities of the extremities and vice versa.

Abnormality of the anterior part of the skull associated with congenital talipes and ulnar deviation of the hands was reported by Freeman and Sheldon (1938) A curious case of abnormality of the extremities and gross maldevelopment of the skull—open sutures and projection of the cervical spine into the base—has been described by Hajdu and Kauntze (1948)

We have seen mild acrocephaly in a lad with generalised gigantism and adolescent kyphosis with exceptionally marked osteochondritic changes in the spine. We have also seen digital impressions in the skulls of two brothers in the care of Dr R. Lightwood with signs of the Morquio-Brailsford type of osteochondro-dystrophy a third member of the family of eight children also had this affection but without obvious impressions in the skull In all three cases the skull was dolicho-cephalic, not acrocephalic in shape. The case we report and illustrate with cystic changes in the metaphyses appears to be unique and to constitute yet another example of the many types of abnormality of the extremities which may be associated with acrocephaly

Radiological appearances—In addition to the abnormal shape of the vault and base the bones are thin and digital impressions" are a striking feature of radiographs of the skull in those not past the years of childhood In some of the impressions the bones may be actually perforated The sella is usually of normal size but in some cases it has been enlarged. The air sinuses are not visible In the extremities the type and extent of the bony

malformations present are revealed in some cases these are gross (Smith 1930 Gray and Dickey 1947)

In the *lacuna skull* (Lückenschadel of Engstler 1905) the cause of which is unknown clear areas somewhat similar to digital impressions are distributed over the calvaria but the bone between the clear areas is noticeably dense

Laurence-Moon Syndrome is the name attached to another uncommon condition in which polydactyly or other peripheral malformations occur associated with obesity retardation of mental and sexual development atypical retinitis pigmentosa and a certain degree of dwarfism. The subject was reviewed by Cockayne *et al* (1935) and a case showing gross malformation of the legs was reported by Levinston (1937)

Pleonosteosis of Léri (1921)—This is a very uncommon hereditary condition characterised by " broadening and deformity of the thumbs, flexion contracture of the fingers thickening and stiffness of the toes limited movement of other joints, shortness of stature and a Mongoloid facies. This description is quoted from a recent review by Watson-Jones (1949) who reported four cases the first to be published in this country One of these cases was complicated by bilateral compression of the median nerve in the carpal tunnel and bilateral plantar digital neuromata.

It is not proposed to discuss the many other different types of malformation of the hands associated with other errors of development which have been reported, some of them hereditary

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CASE 82—ACROCEPHALO-SYNDACTYLY

(Fig 240) Female aged five months. Typical tower head highest point of cranial vault corresponds to anterior fontanelle which is tense and protruding Palpebral fissures oblique downwards and outwards. Exophthalmos. Mentally normal. Limitation of movement at the elbows. Both hands and feet show syndactyly First digits in hands and feet partly separated from the others. In hands middle three digits fused and have a common nail. Fifth digit separated at tip. Four outer toes joined. Radiograph of skull showed digital markings and premature closure of sutures. In the hands and feet malformation and deficiencies are seen. (Reported by Dr Jean Smith 1930)



FIG. 249

Case 82—Drawing of radiographs of feet showing the syndactyly and the abnormalities of the bones Note the absence of some phalanges. (After Dr Jean Smith)

CASE 83—ACROCEPHALO-SYNDACTYLY

(Fig 250) Male aged three years. Typical tower head. Cleft palate. Bilateral symmetrical deformities of extremities. Mitten-hands and sock feet. Radiographs showed slight digital markings in middle and posterior parts of the vault middle fossa very deep and much enlarged incomplete synostosis of coronal suture and partially open accessory coronal suture in mid-parietal region. Malformations and deficiencies in bones of hands and feet. Absence of some phalanges. (Reported by Gray and Dickey 1947)



FIG. 250

Case 83 Drawing of radiographs of sock feet, showing abnormal toes the first digits, and absence of one row of phalanges (After Gray and Dickey)

CASE 84—ACROCEPHALY with abnormalities of the extremities

(Figs. 251 to 257.) C. C. male aged ten years. Stature below the average. Hands and fingers stubby. Some bow leg due to tibiae. Slight thickening of lower femoral and lower tibial metaphyses. Limitation of extension of elbows. Head increased in height, decreased in circumference. Hollow above each orbit. Heavy facies. Palate normal. Eyes prominent. Great thickening of the alveoli in both jaws. Never had any upper teeth. Two lower incisors erupting a quarter-inch behind healed sockets of temporary teeth. Intelligence somewhat low. Two siblings normal. X rays showed typical digital markings all over skull. Pituitary fossa enlarged. Permanent teeth apparently well calcified. Bones of hands definitely abnormal in shape; suggestion of V-shape of epiphysial lines at bases of phalanges. Lower radial and ulnar epiphyses unusually thin. Some clear areas in necks and trochanteric regions of femora. Definite cystic formation in lower metaphyses of both femora; similar but much less marked changes in upper metaphyses of tibiae. Lower tibial epiphyses on inner side and adjacent portions of metaphyses are rather fluffy. Tarsal bones and first metatarsals show some abnormality in shape.

At twenty-four years, a thick-set man. Height 49 inches. Intelligent. Works as draughtsman. Legs rather short. Limitation of extension of elbows and knees. Hands broad and fingers very short and thick. Nails very short and broad. Rather abrupt dorsal scoliosis. Skull markedly oxycephalic. Says he has never had any teeth; refuses to use dentures. Radiographs show finely mottled skull of typical shape; no obvious digital impressions visible now. Cystic changes in the lower femora and upper tibiae are no longer present. Texture of long bones is irregular and differentiation of cortex and medulla is often imperfect, particularly in the upper limbs. (Under Mr H. L.-C. Wood.)



Fig. 251

Case 84—Lateral view of skull at ten years, showing abnormal shape and digital markings. Note the enlarged sella.

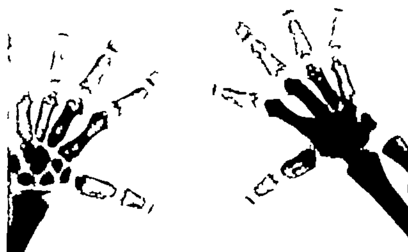


Fig. 252

Case 84—Hands at ten years, showing unusual shape of many of the bones and abnormal epiphyses, including those of the radius and ulna



Fig. 253

Case 84—Femora at ten years, showing the cystic appearance of the lower metaphyses



FIG. 254

Case 84—Photograph at twenty four years, showing the posture shape of the head and the st bby fingers



FIG. 255

Case 84—Skull at twenty four years, showing the tower" shape and curious mottling. Note the many well calcified unerupted teeth.



FIG. 256

Case 84 F mora t twenty four ears, showing the disappearance of the cystic hanges in the lower ends nd the bnormal texture



FIG. 257

Case 84—Hand t twent four ears, showing the abnormal shape and texture of the bones.

CHAPTER 19

ENGELMANN'S DISEASE

Synonyms:

Osteopathia Hyperostotica (Scleroticans) Multiplex Infantalis (Engelmann)
Progressive Diaphysial Dysplasia (Neuhauser *et al.*)

This uncommon condition, recognised as a clinical entity only in recent years, is characterised by symmetrical fusiform enlargement and sclerosis of the shafts of the major long bones, associated in the majority of cases with changes in the skull. Though described by Engelmann in 1929 only about fifteen other cases seem to have been published if doubtful cases are excluded. In 1920 Cockayne showed a case "for diagnosis," a boy of nine years with symmetrical hyperostosis of some of the long bones and changes in the skull; we now think this boy, whom we saw while he was in hospital, is the first case to be reported of this condition. What appears to be an allied condition was described by Ribbing (1949) under the title of Hereditary Multiple Diaphysial Sclerosis; he reports a family with four members affected—one seems questionable—and quotes Camurati (1922) who reported a father and son with a similar affection.

Hereditary and familial influences play no part in the incidence.

Sex—Males are more commonly affected than females.

Age—The majority varied in age from four to ten years. A child of one year whom we should place in this group was reported by Hirsch (1920). Under the title of generalised leontiasis ossea, Garland (1946) reported a possible case, a man aged thirty years, while Michaelis (1949) published an unquestionable case aged twenty-five years. Stronge and McDowell (1950) one of twenty-eight years, and Fritsch (1932) one of twenty years.

Etiology—The cause is entirely unknown. There is an inclination towards regarding it as a congenital developmental error.

Signs and symptoms—There are no specific symptoms. Some complained of pain in the legs; many are weak and waddle; some are said to have always had a peculiar gait; they tire readily. One had had difficulty in walking for four years. Some have been thin and long-limbed. Malnutrition is not uncommon. Headache was complained of in only one instance. The spleen was enlarged in Engelmann's case. Tenderness of a femur was reported by Sear (1948). The thickening of the shafts of the long bones can be felt. Various minor neurological signs have been reported, but none of clinical importance.

Blood examination has revealed nothing significant. The alkaline phosphatase was raised in one case (Bingold 1950).

Radiological appearances—The long bones affected most often are the femora, tibiae, radius and ulna, and the fibula. The clavicles and humeri are less commonly involved; in single instances the ilium, ischium, scapula, mandible and some metacarpals have been affected. In most cases the hands and feet, ribs and spine escape. The first cervical vertebra showed changes in a boy of ten years (Sear 1948). In a long bone the changes consist of a more or less fusiform enlargement of the shaft. The surface of the enlargement is usually smooth. The length of the shaft affected varies, but most frequently the middle two fourths are partially or wholly involved. In a few cases the lower half of the femoral shaft has been enlarged and a second smaller fusiform lesion has been present in the upper third in both legs (Sear 1948, Riley and Schwachman 1943, Caruccio 1949). In Riley and Schwachman's second case both tibiae and fibulae showed double enlargements in the later films. In most

cases the enlargement is associated with increased density In some this seems no more than the additional bone would account for the new bone being irregular in density In most cases, and probably in all eventually there is no doubt about the sclerosis. The appearance suggests the cortex is thickened both within and without and there is never a separate layer of subperiosteal new bone The medullary canal is reduced in size. The skull was affected in about two-thirds of the cases there is increased density of the base or the frontal region and usually of both The inner table in the frontal region showed a dense thickening in two cases (Michaelis 1949 Fritsch 1932)

Progress—Definite extension of the changes in the bones and involvement of additional bones was noted in several cases watched for a few years.

Pathology—Biopsy was performed in at least five cases and sections showed nothing but sclerosis. In Bingold's case (1950) the bone was exceptionally hard. Some fibrosis, with ample numbers of osteoblasts and osteoclasts, is reported by Neuhauser *et al* (1948) and fibrosis of the marrow was noted by Holt (1940) in a case referred to as Juvenile Paget's disease but which we think might be included in the Engelmann group

Diagnosis—Before it is realised that more than one bone is affected osteomyelitis will naturally have to be considered. Leucocytosis with or without fever should, of course, be present The only condition at all closely simulating the radiological picture with several long bones showing changes is infantile cortical hyperostosis. This occurs within the first year of life is accompanied by fever as a rule, and before many months have elapsed it shows clear signs of recovery with disappearance of the radiological changes. In this condition the mandible is frequently affected. Osteopetrosis should be distinguishable without difficulty increase in size coupled with increased density is seen towards the ends of the shafts producing clubbing When the middle portions of the shafts show increased density rather than the ends the dense portions are not enlarged. Even when there have been intermissions in the formation of petrosed bone the complete radiological picture is entirely different from that of Engelmann's disease

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CASE 85—ENGELMANN'S DISEASE

(Fig 258) D T., male aged eight years. Always had a peculiar gait. At three years legs seemed unduly weak and knee jerks were not obtained. Strength improved and later muscular dystrophy and organic nervous disease were excluded by a neurologist. Two years ago radiographs showed coxa valga and expansion of femoral shafts. On examination, has lurching gait. Trendelenburg negative. Bow legs due to deformity in upper thirds of tibiae Thickening of shafts of femora easily felt No other bones thickened. Some fixed flexion of both hips and both knees Feet flat with excessive dorsiflexion and limited plantar flexion. Knee jerks and ankle jerks obtained. Plantar responses extensor Slight dorsal kyphosis. Muscles small but fairly strong Blood nothing significant. Alkaline phosphatase 11 8 units later 6·8 units. Radiographs showed symmetrical fusiform enlargement of the femoral shafts. No other lesions discovered but skeleton generally somewhat lacking in density Nine months later radiographs showed a little increase in size of the enlarged portions of the femoral shafts One sister shows no sign of the disease

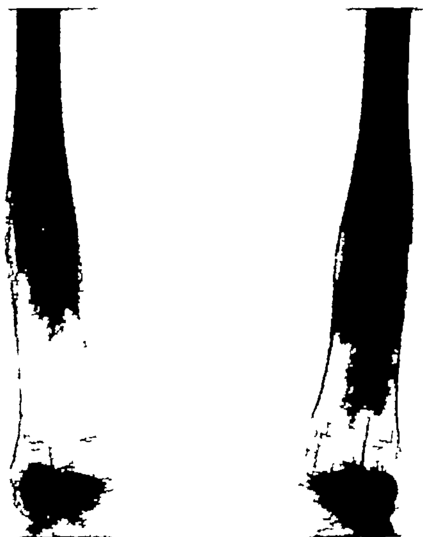


Fig 258

Case 85 —Femoral shafts showing the symmetrical enlargements and increased density

CASE 86—ENGELMANN'S DISEASE

(Figs. 259 to 261.) A. G., male, aged nine and a half years. Admitted for loss of weight and incontinence for past five years. Thin undersized boy with slender limbs. Mentally dull. Eyes prominent. Radiographs showed marked thickening of the frontal bone, abnormal density of the base of the skull and irregular thickening of the femoral shafts. Similar but more limited changes were seen in the shafts of both humeri, both tibiae and one fibula. Feet and hands normal. Temperature normal. No incontinence. Wassermann negative; father's blood also negative. Two older siblings normal. (Under Dr. E. A. Cockayne. Reported in Proceedings of the Royal Society of Medicine 1920.)



FIG. 259

Case 86—Femora showing the symmetrical cortical thickening of the shafts, with increased density and narrowing of the medullary canals.



FIG. 260

Case 86—Humeri showing symmetrical cortical hyperostosis on the inner sides of the lower halves of the shafts.

FIG. 261

Case 86—Skull showing thickening of the frontal and some increased density of the base.



CHAPTER 20

FIBROCYSTIC DISEASE OF BONE

In arriving at our present knowledge of the conditions characterised by multiple skeletal lesions of which the chief feature is fibrosis, certain contributions have been outstanding. It is generally agreed that the first step was made by von Recklinghausen in 1891 when among cases of various types he described two of generalised osteitis fibrosa, a condition to which his name is still attached. In 1904 Askanazy reported a case of this affection in which a parathyroid tumour was discovered after death. The next step, one of enormous importance, was made by Mandl in 1926 when he successfully removed a parathyroid tumour from a case with typical bone changes.

In this country there has been conspicuous work by three men, Donald Hunter, Turnbull and Elmslie, the first two with particular regard to hyperparathyroidism. Among several papers by these authors two may be mentioned here. In an exhaustive article on hyperparathyroidism Hunter and Turnbull (1931) referred to the "more common" cases with multiple lesions in the bones not due to hyperparathyroidism and therefore not associated with disturbance of calcium metabolism and generalised osteoporosis. In 1933 Elmslie classified fibrocystic disease of bone as follows: 1) bone cysts, 2) osteoclastoma and osteoclastomatous cysts, 3) diffuse fibrosis of bone, 4) generalised diffuse fibrosis of bone and 5) hyperparathyroidism. In opening a discussion on the subject in 1934 he stressed the similarity of the changes in the two types of "diffuse fibrosis" with single and multiple lesions respectively; concerning the latter group he referred to two important points—a tendency towards a unilateral distribution of the multiple lesions, and involvement of the skull in many of the cases. Though not the first to report precocious puberty associated with bone lesions, Albright and his associates in 1937 described the syndrome (now commonly known by his name) in which the multiple bone lesions are associated with areas of pigmentation of the skin and, in females, with precocious puberty. In recent years there has been a tendency to regard the two conditions—multiple bone lesions without signs of hyperparathyroidism (known to many as osteitis fibrosa disseminata) and the Albright syndrome—as one and the same. In 1938 Lichtenstein reviewed the subject, his classification being essentially the same as Elmslie's, and suggested "polyostotic fibrous dysplasia" as a suitable name for the cases of multiple diffuse fibrosis of bone without signs of hyperparathyroidism. The term has become increasingly popular in recent years and therefore has been adopted by the present writer.

There are, of course, several other conditions in which fibrosis forms a part—in some a conspicuous part—of the pathological changes in the bones. In Paget's disease fibrosis of the marrow is the fundamental change, as it is also in leontiasis ossea, whether this occurs as a solitary affection of the skull or as one of several skeletal lesions in polyostotic fibrous dysplasia. Among other affections in which fibrosis of bone is met with may be mentioned renal rickets and osteopetrosis; it has even been reported associated with generalised thyrotoxic osteoporosis. Fibrosis of the marrow in relation to increased and decreased density of bone we discussed in 1939.

POLYOSTOTIC FIBROUS DYSPLASIA

Synonyms—Multiple Diffuse Fibrosis of Bone Osteitis Fibrosa Disseminata

SUB-GROUP ALBRIGHT'S SYNDROME

This condition is characterised by multiple lesions in the skeleton due to fibrous dysplasia of the bones but without the general decalcification and disturbance of calcium metabolism indicative of hyperparathyroidism. In a proportion of the cases, at most one-third there are in addition areas of pigmentation of the skin and, almost exclusively in females, precocious puberty giving the so-called Albright's syndrome. Except that the cases exhibiting the features of this syndrome usually show more advanced changes in the skeleton than those showing nothing but the bone lesions, there is no essential difference between the two groups so far as the skeleton is concerned, and, as stated above they are now regarded as variations of one and the same condition. Besides the papers already referred to valuable articles have been published by Falconer *et al* (1942) Dockerty *et al* (1945) and Murray *et al* (1946)

Hereditary and familial influences—Neither of these affect the incidence.

Sex—Both sexes are affected, females slightly more frequently than males.

Age—Though definitely an affection of childhood it is often not recognised till much later in life Reviewing some ninety cases collected from the literature and elsewhere, we found that in those without pigmentation the age at which the first signs appeared was ten years or younger in about one-half the youngest being two years. In those showing pigmentation, with or without sexual precocity in addition, the age of onset was ten years or younger in two-thirds the youngest being four months old. Many of the older cases had very long histories

Etiology—Many suggestions have been made as to the causation but none has been generally accepted. The difficulty is to find a common cause not only for the apparent endocrine error and for the bone lesions but also for the tendency of these lesions to be unilateral in some cases at any rate Many feel the fundamental error must be congenital, and the hypothalamus is suspected as the seat of the primary fault by several authors. In the small number of cases in which signs have developed after icterus neonatorum, blame for the bone changes has been placed on the liver which is said to have failed to store and utilize vitamins (Braid 1939)

Distribution of the bone lesions—The number of bones affected varies considerably there may be only two or three or there may be many Cases with only a single bone affected were excluded from our series, with one exception. This was a male of ten years with a large area of pigmentation on the back and with the left femur the only bone affected by fibrosis (Dockerty *et al* 1945) Three additional monostotic cases displaying pigmented patches have been published one by Jaffe (1946) and two by Russell and Chandler (1950) Though in the cases with Albright's syndrome the bones are generally more severely affected than in the others, there are many exceptions. In rather more than half the cases in both groups, the bone lesions are predominantly and occasionally completely unilateral in distribution When the lesions are bilateral they are not symmetrical. Sometimes they are almost or completely monomelic this limited distribution we found in one case in every seven of those without pigmentation and one in ten of those with the Albright syndrome The bones affected are particularly the major long bones and the proximal bones more than the distal. Of the individual bones the femur is affected in almost every case the humerus tibia and fibula radius and ulna metacarpals, metatarsals and phalanges are all frequently the seat of lesions In the hand it is common to find two or three metacarpals affected, the other bones being normal a similar irregular distribution is seen in the foot The skull is affected in about one-third of the non-pigmented cases and in two-thirds of the pigmented the changes are indistinguishable from those designated leontiasis ossea. The pelvis vertebrae tarsal and carpal bones sternum and mandible are affected less frequently A case with changes in

both clavicles, some ribs and cervical vertebrae in addition to the skull and mandible has been reported by Gemmell (1935)

Signs and symptoms—The onset is insidious. Attention may be called to an affected bone by a variety of incidents such as a fracture the appearance of deformity due to either bending or local enlargement of a bone or the development of asymmetry of the face and skull. Pain and stiffness in a limb are less common initial symptoms. Minor trauma may precede the development of deformity without causing a definite fracture. Progressive deformity and shortening of a limb may be observed later Only exceptionally is an affected bone longer than its fellow When changes in the skull, face or jaw occur exophthalmos and even gross displacement of an eye may gradually develop. Asymmetry of the face may progress till hideous or grotesque deformity is produced. Nasal obstruction may be complained of when the facial bones are affected. Pain is not a prominent symptom as it is so often in hyperparathyroidism nor does the patient feel ill and feeble as he so commonly does in that condition.

The changes in the bones and the resulting deformities usually progress slowly until skeletal *growth ceases when there is commonly a definite halt. If both legs are severely* affected the patient may be permanently crippled.

Albright's syndrome—Though as already stated, Albright's syndrome is met with usually in the more severe cases, it has often been recognised in the very young when the bone changes were still in an early stage of development or even confined to one bone. In the series reviewed we found that about one-third of the cases exhibited signs of the syndrome but since these are more likely to be recorded than cases with bone lesions only this proportion is probably too high.

Pigmentation—Pigmented areas are practically always seen in these cases, both sexes being affected. The areas are smooth and without local thickening of the skin. Common sites are the lower back, buttocks and thighs. The size of the areas varies considerably but they may be large They exhibit a slight tendency to occur on the side of the chief osseous lesions.

Sexual precocity—This is almost exclusively found in the female patients who exhibit pigmentation and in them it is rarely absent An exception was a girl of eighteen years with pigmentation and skeletal precocity but without sexual precocity (Falconer *et al* 1942) The earliest age at which signs of sexual precocity have appeared is four months (Freedman 1932) in three other cases it was apparent by the third year In males sexual precocity is usually absent but signs of this have been seen in a few cases (Lange 1938 Falconer *et al* 194. Warrick 1949—two cases) A lad of sixteen displayed female characteristics as regards his voice development of the breasts and pubic hair (Moehlig and Schreiber 1940) but there is no mention of pigmentation in this report.

Skeletal precocity—This is more common than sexual precocity The children grow too fast and appear tall for their age but premature fusion of the epiphyses occurs and growth ceases too early with the result that their permanent height may be below the average. Most of the women exhibiting the full syndrome are short in stature

Blood examination—In most cases the calcium and phosphorus levels are normal. The serum calcium may be a little high in spite of the absence of general decalcification of the skeleton. The cholesterol is in normal amounts as a rule and has been high only in a few cases (Snapper 1949) The alkaline phosphatase may be normal but is frequently high particularly after a fracture The excretion of calcium in the urine is normal. Traces of Bence Jones albumose and of albumin were present only in one typical case of Albright's syndrome (Murray *et al* 1946)

Radiographic appearances—The changes in the bones are seen in the shafts and metaphyses. Only rarely do the epiphyses show changes after they have fused to the shafts they may exhibit some irregularity of density or mottling or the lesions in the shafts may extend into them The lesions are essentially endosteal in origin and vary considerably in appearance. There may be only a small lesion somewhat cyst like or perhaps two separate lesions of this

type without distortion of the surface of the bone at the other extreme there may be complete involvement of the whole shaft which is both enlarged throughout and deformed and perhaps shows signs of old or recent fractures. A case with exceptionally severe changes in the bones was recorded by Bradfield (1931) The part of a shaft showing fibrotic changes may be sharply marked off from the rest which is normal. It is common for example in the upper part of the femur to see the shaft enlarged and showing only a thin cortex, the density for the most part being uniform except for a few scattered patches of increased or decreased density The ground glass appearance with uniform medium density so typical of diffuse fibrosis is frequently seen in the metatarsals and metacarpals, the shafts of the affected bones being somewhat enlarged. Only occasionally is there a local fusiform enlargement containing clear areas strongly suggestive of cysts. An enormous loculated "cyst" of a rib has been reported by Jaffe (1946) Subperiosteal or cortical cysts not infrequently seen in hyperparathyroidism, are distinctly rare Sometimes increase in density is the chief feature usually but not invariably this is accompanied by some enlargement of the shaft. The density often ends in three or four broad streaks towards one or both extremities of the bone. The larger and more extensive lesions, accompanied by deformity are seen typically in the upper half of the femur though also met with in other major long bones. Occasionally the fibrotic portion of a bone displays a mottled appearance. An important point to keep in mind is that the unaffected bones or parts of bones are normal in appearance and density There is an absence of the intense generalised osteoporosis seen in hyperparathyroidism a mild degree of osteoporosis may be seen but only in a case that has been severely crippled for some months.

Skeletal precocity may be apparent in cases with pigmentation and premature fusion of the epiphyses may occur

In the skull the changes also vary considerably The commonest change especially in the early stages is local thickening with irregular mottled increased density Commencing in the maxilla, the malar region or elsewhere in the cranium the changes gradually spread. Islands of sclerosis occur here and there and increased density is common at the base Only exceptionally are cyst like holes seen in the calvarium and even more rarely do blister like cysts form on the surface There is no generalised decalcification The changes are frequently unilateral, particularly in the early stages, the orbit and maxilla on one side only being affected. Occasionally the whole vault base and facial bones are involved (*vide* leontiasis ossea) Gemmell's case already referred to was exceptional because it showed increasing thickness of the inner rather than the outer table over a period of years with apparent reduction in size of the cranial cavity

Progress—As a rule the changes are progressive especially in the more severe cases but they tend eventually to be arrested as skeletal growth ceases. Though further extension may come to an end the abnormal areas of bone do not consolidate but remain as weak spots in the limbs. Delayed increase in size of a lesion occasionally happens even in middle life In one case the increase was rapid (*Jaffe 1946*)

Complications—Fractures are common but unite readily Thyroid enlargement may be present in severe cases and exophthalmic goitre has been reported in a few being associated with basophilic adenoma of the pituitary in one case (Sternberg and Joseph 1942) Acromegalic features and severe failure of vision were present in two cases reported by Falconer *et al* (194[illegible]) Arterio-venous aneurysms occurred in one case (Stauffer *et al* 1941) In another very remarkable case a man of fifty-seven years soft tissue tumours which were cystic and apparently similar to ganglia were associated with widespread cystic changes in the bones including the skull, all the lesions being on one side (White 194[illegible]) Sarcoma developed in an affected bone in two cases (Coley and Stewart *194[illegible]*) Osteogenic sarcoma of a tibia with other bones showing fibrosis was reported by Jaffe (1946) This author also reported paraplegia developing in middle life in a case of polyostotic fibrous dysplasia in which the spine was

affected. The present writer published a fatal case of renal rickets in which several bones, including the skull, showed diffuse fibrotic lesions no parathyroid tumour was discovered at autopsy (Fairbank 1930)

Pathology—The essential change is the replacement of bone by relatively avascular fibrocellular tissue. This change occurs in two forms. In one the bone is replaced by yellowish or greyish white fibrous tissue sometimes speckled with red and containing some gritty bone in the other form all but a thin shell of cortex is replaced by fine-mesh cancellous tissue in which the spaces are filled by fibrous tissue. Precisely similar changes may be present when only a single bone such as the femur is affected by fibrosis. The density of the fibrous tissue varies considerably from soft and cheesy to very dense. Many whorls of fibroblasts are seen in most cases (Valls *et al* 1950) Though the fibrous tissue contains a considerable amount of bone it can be cut readily with a knife. The younger the lesion the greater the number of fusiform spindle cells in the fibrous tissue, the older lesions being less cellular Though the cortex is absorbed from within, osteoclasts are few and osteoclastomata are very seldom seen—an important difference from the condition found in hyperparathyroidism Osteoblasts are present, and there is a varying amount of new bone formation. Osteoid tissue and irregular areas of woven bone are formed as they are in hyperparathyroidism and in Paget s disease. Cartilage is seen occasionally more often in the later stages (Elmslie 1935) Cysts if present at all, are usually small, and are the result of degeneration. Apart from noticeable scarcity of osteoclasts the histology in these cases differs from that in hyperparathyroidism in the absence of survival of some of the original trabeculae and in the haphazard arrangement of the fibre bone trabeculae (Robb-Smith in Falconer *et al* 1942) A few but only a few foam cells have been found at sites of degeneration in typical cases and these were regarded as secondary (Lichtenstein and Jaffe 1942 Dockerty *et al* 1945) Foam cells were found in a girl of seventeen years displaying the typical Albright syndrome (Sanchez Lucas and Freixa 1949) The difficulty of distinguishing cases of fibrosis from lipoidosis has been stressed by Snapper who pointed out that because the foam cells in lipoidosis may be gradually swamped by the fibrosis, it is advisable to select reasonably young lesions for histological examination he now admits that the finding of foam cells does not exclude a diagnosis of polyostotic fibrous dysplasia (Snapper 1949) The changes in the skull are those seen when there are no lesions elsewhere in the skeleton, that is, in the cases usually designated leontiasis ossea there is fine-mesh cancellous bone with diffuse fibrosis of all the marrow spaces In Paget s disease the fibrous tissue is less dense and more myxomatous, and may be extremely vascular with many osteoclasts present the new trabeculae show a greater tendency to a mosaic arrangement

The pigmented skin is normal except for an excess of pigment, found chiefly in the basal layer but occasionally in the granulosum. Haemosiderin may be found in the reticulo-endothelial cells. In a few severe cases some enlargement of the parathyroid glands has been found this enlargement was regarded as secondary it was not accompanied by generalised osteoporosis

Diagnosis—When there are only one or two lesions present the diagnosis may be difficult or impossible without biopsy but as a rule it is easy From the cases which do not display the typical Albright syndrome *hyperparathyroidism* may be distinguished by the age of the patient—it is uncommon in childhood—by the high serum calcium with negative calcium balance the generalised osteoporosis and the renal lithiasis, besides which pain is a far more prominent feature and the patient often feels ill and weak. *Xanthomatosis* may be difficult to exclude In Hand Schuller-Christian disease the clear punched-out lesions in the skull are typical in th fibrosis cases clear holes or patches in the skull are uncommon and never as sharply defined as in lipoidosis The diagnosis from *melorheostosis* may be somewhat difficult when the fibrosis is associated with increased density perhaps ending in streaks in one metaphysis and the distribution f the fibrosis happens to be monomelic. Patches of intensely

dense bone in the hand or foot should settle any doubts in favour of melorheostosis the changes caused by fibrosis in the extremity of a limb are usually of the ground glass type and equally characteristic.

Paget's disease should give rise to no difficulty unless the skull is alone affected the honeycombed appearance of an affected long bone the obvious new bone formation on the surface and the characteristic pointed extremity of the spreading lesion should remove all doubts as to the diagnosis.

Eosinophilic granuloma usually affects one bone only but multiple lesions have been reported (Platt and Eisenberg 1948 Ponseti 1948) *Tuberous sclerosis* may affect a major long bone but this is quite exceptional (Ackermann 1944)

In *neurofibromatosis* bone changes somewhat similar to those described in this chapter particularly increased density in the shaft of a long bone with or without cortical cysts may be seen but the diagnosis should not be difficult. Thannhauser (1944) considers that the two conditions multiple diffuse fibrosis and neurofibromatosis, are related.

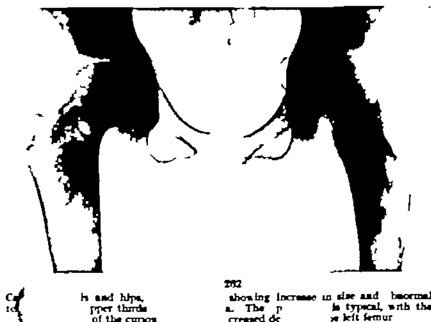
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CASE 87—POLYOSTOTIC FIBROUS DYSPLASIA

(Figs. 262 to 260) Male aged nine years. Admitted to hospital with vague history of getting tired quickly especially so since suffering from a combination of infectious diseases eight months before. Limping for previous two years. One year previously radiographs revealed changes in the left femur Healthy-looking boy Many very small pigmented spots scattered over the face body and limbs. Thickening of trochanteric region of left femur upper part of left tibia and first metatarsal of left foot. Second and third toes of right foot longer than corresponding toes on opposite foot the heads of metatarsals prominent Left leg at least half an inch longer than right, mostly due to tibia. Circumference of left thigh and calf greater than those of right. Complete radiographic examination revealed typical changes of varying density mostly but not exclusively in the bones of left leg Bones affected were left femur tibia first metatarsal (which was elongated) and its corresponding phalanges. In the right leg the upper part of femur the second and third metatarsals and their phalanges showed changes. Special features were the increased density at several spots, particularly in the left tibia, the striated or streaky appearance in this bone and in the femur near the knee joint, and curious dense lines in the upper third of this femur No definite changes found in the skull or the upper limbs. There was no generalised decalcification of the skeleton. Serum calcium was slightly raised varying from 11·0 to 12 5 milligrammes per 100 cubic centimetres, but complete examination of the calcium metabolism gave normal results. Blood examination otherwise negative. Biopsy of left femur and tibia revealed diffuse fibrosis of the marrow there was some myxomatous change, and a few small cysts were seen here and there.

Radiological re-examination five years later showed a little extension of the changes. In the upper part of both femora the appearance was more suggestive of cystic changes and more of the neck of the left femur was involved. Deformities in the left femur and tibia showed some increase they were corrected by osteotomies. Later a pathological fracture occurred at the mid-shaft of the femur at the site of pronounced cystic change. At the age of seventeen the lesions were even more cystic in appearance especially so in the left femur extension of the changes into the inner condyle and possibly into the head of this bone were seen. (For the later history and radiographs we are indebted to Mr Norman Capener)



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C... ...s and hips, showing increase in size and ...bnormal ...a. The p... ...s typical, with the ...pper thirds ...creased de... ...e left femur ...of the curious



Fig. 283

Case 67—Knee joints at nine years, showing enlargement of the shafts of the left femur and tibia, and increased density of these bones ending in streaks in the metaphyses

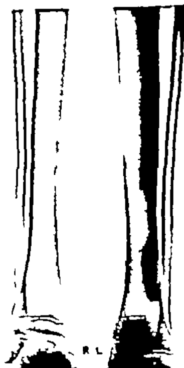


Fig. 284

Case 67—Tibiae and fibulae at nine years, showing the distribution of the increase in size and density in the left tibia.



[*Left*] Fig. 285 [*Right*]

Case 67—Feet at nine years, showing enlargement and textural changes in certain bones. Note the excessive length and breadth of the left first metatarsal and corresponding phalanges, and similar changes in the phalanges of the second and third toes of the right foot. The shafts of the second and third metatarsals of this foot are enlarged, but show no excess in length.



FIG. 266

Case 87—Hips at fourteen years, showing that the changes in the femora have become more cystic in appearance the left femur has developed a deformity



FIG 267

Case 87—Left femur at fourteen years, showing "cystic" changes middle of the shaft, the site of a pathological fracture later



FIG. 268

Case 87—Left knee at fourteen years, showing more curvature of the tibia and well-marked striation of the femoral and tibial metaphyses.

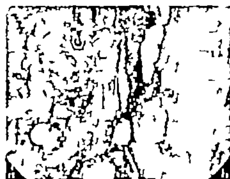


FIG 269

Case 87—Section of left femur showing (a) irregular cancellous bone with all marrow spaces filled with cellular fibrous tissue (b) dense cortex. (Magnification, ×40)

CASE 88—POLYOSTOTIC FIBROUS DYSPLASIA (Unilateral distribution with leontiasis ossea)

(Figs 270 to 276.) Male aged six and a half years. A lump on left side of head and some proptosis of left eye noticed for previous nine months. Child nervous and anaemic. Hard swelling of skull in left temporal region not tender Family history negative. Radiographs of the skull showed increased density and slight thickening in the left temporal and malar regions and of the left maxilla. In 1922 biopsy by Mr (now Sir Lancelot) Barrington Ward. Fragment of bone removed was cancellous and fairly hard. Section showed fine cancellous bone with fibrosis of the marrow and numerous spindle cells and a few giant cells indicating leontiasis ossea. Radium was inserted on two occasions. Blood examination negative. Serum calcium 11·2 milligrammes phosphorus 3 18 milligrammes per 100 cubic centimetres. Phosphatase slightly raised. Further radiological investigations showed lesions in left arm and leg, involving the humerus, third, fourth and fifth metacarpals, some proximal and middle phalanges, femur tibia and fibula. No generalised osteoporosis. Progress in the bone lesions was more obvious in the skull than elsewhere and by 1926 the increase was marked the left eye had become more prominent The left forearm bones still appeared free from lesions and the hand showed little change By 1933 at the age of seventeen years, there were further striking changes in the skull, and the deformity of the face was gross the left eye was displaced forwards and downwards fortunately without interference with vision. In addition to the frontal and anterior part of the parietal the occipital had become involved. The upper parts of the skull were mottled In the left arm the radius and ulna now showed cystic changes with some sclerosis. Affected bones in the hands showed some advance in the changes but no additional bones were involved. In the leg the lesions also showed advances the three middle metatarsals and their corresponding phalanges were now affected.



Fig. 270

Case 88—Skull at six years showing early thickening of the left malar and temporal regions there is increased density involving the left maxilla. The appearance is typical of early leontiasis



Fig. 271

Case 88—Legs at six years showing early changes in left tibia and fibula—diffuse irregular sclerosis in tibia, enlargement and cyst-like changes in fibula



Fig. 272

Case 88—Antero-posterior view of skull at seventeen years, showing considerable extension of the changes, no longer confined to the left side; there is greater irregularity in the density of affected bones. (Compare with Fig. 270.)



Fig. 273

Case 88—Lateral view of skull at seventeen years, showing irregular increased and decreased density of affected bones including the left maxilla. Note involvement of the occipital, and absence of the frontal sinuses.



Fig. 274

Case 88—Forearms at seventeen years, showing the cystic changes, without enlargement, in the shafts of the left radius and ulna and irregular increased density in the left humerus.

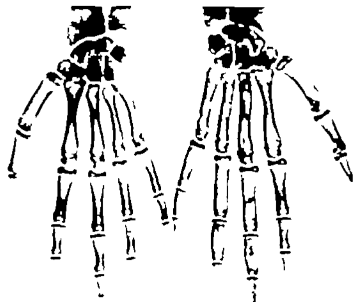


Fig. 275

Case 88—Hand at seventeen years showing in the left, enlargement and [illegible] rity of changes in density of the three [illegible] metacarpals and their phalanges. Note that the carpus, thumb and first finger of the left hand and the whole right hand are normal.



Fig. 272

Case 88—Antero-posterior view of skull at seventeen years, showing considerable extension of the changes, no longer confined to the left side there is greater irregularity in the density of affected bones. (Compare with Fig 270)



Fig 273

Case 88—Lateral view of skull at seventeen years, showing irregular increased and decreased density of affected bones, including the left maxilla. Note involvement of the occipital and absence of the frontal sinuses.



Fig. 274

Case 83—Forearms at seventeen years, showing the "cystic" changes, without enlargement, in the shafts of the left radius and ulna and irregular increased density in the left humerus.

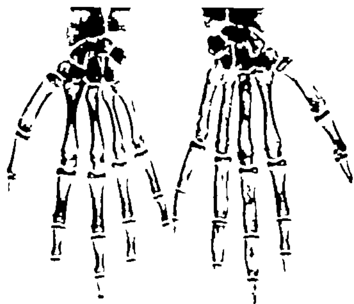


Fig. 275

Case 83—Hands at seventeen years showing, in the left, enlargement and variety of changes in density of the three inner metacarpals and their phalanges. Note that the carpus, thumb and first finger of the left hand and the whole right hand are normal.



FIG 276

Case 88—Legs at seventeen years, showing enlargement of the shafts of the left tibia and fibula, with a mixture of cyst-like areas and increased density Note the absence of signs of osteoporosis in the right leg.

CASE 89—POLYOSTOTIC FIBROUS DYSPLASIA (Unilateral distribution)

(Figs. 27 to 280) Girl aged twelve years. At the age of three years she fell and broke her right femur no other fractures. Right femur found thickened after recent fall on hip radiographs revealed the dysplasia, with partial fracture of this bone and lesions in several other bones in the right arm and leg No asymmetry of the face or skull but there was a suspicion of increased density in the right malar region in an antero-posterior radiograph. Right leg one-quarter of an inch short Blood examination leucocytes 9 400 per cubic millimetre lymphocytes 45 5 per cent. Serum calcium 11 1 11·4 and 10·2 milligrammes per 100 cubic centimetres on three occasions. Plasma phosphorus 4 70 milligrammes per 100 cubic centimetres. Phosphatase 1·03 (normal by this technique 0·25) Complete investigation of calcium metabolism showed some excess of calcium in the urine and also though less marked in the faeces the excess was not considered sufficient to justify immediate exploration of the parathyroids, an opinion kindly confirmed by Dr Donald Hunter

Three years later the case was again investigated, deformity of the femur having increased. Serum calcium was 10·7 milligrammes plasma phosphorus 2 8 milligrammes per 100 cubic centimetres. Investigations of the calcium balance gave normal results.

Eldest of four children. No bone dysplasia in other members of family Most of males in father s family were said to have cataract in some cases congenital.

Bones affected were the tibia fibula, one metatarsal, several phalanges of the foot scapula, humerus, radius and one metacarpal all on the right side. The left humerus showed possible changes. No generalised osteoporosis. Biopsy of femur showed typical diffuse fibrosis. A mass of cartilage was present in a fragment taken from the site of the projection of the outer cortex a doubtful crack is seen in the radiograph.



Fig. 277



Fig. 278

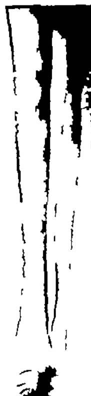


Fig. 279

Case 89—Figure 277 right humerus showing lesions of various kinds distributed through most of the enlarged shaft Note that there is no osteoporosis of the unaffected *upper end of the bone* *Figure 278, right femur* showing increased and decreased density distributed irregularly throughout the shaft. The projection on the outer side marks the site of a possible partial fracture Figure 279 right tibia and fibula showing cystic lesions in the tibia and the ground glass appearance and uniform density of the enlarged middle third of the fibula.

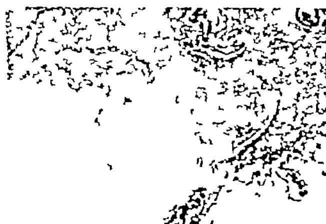


Fig. 280

Case 89—Microscopic section of fragment from femur showing typical fibro-cellular infiltration of the marrow spaces merging with a mass of cartilage an unusual feature (50)

CASE 90—POLYOSTOTIC FIBROUS DYSPLASIA (Albright's Syndrome)

(Figs. 281 to 285) Female aged thirty four years. Healthy till seven years old, when she broke her right femur. While under treatment in hospital for this fracture other fractures occurred in left femur, right elbow and right tibia; later she broke her left wrist. At nine and a half years had operation on right femur for deformity and imperfect union. Was treated on a frame for two and a half years. Has not walked without crutches since right thigh was broken. At seventeen years right femur became tender and two swellings developed. At eighteen years had marked deformity of both legs, and right tibia was tender and painful on bending. Neck explored but no parathyroid tumour found. She married and had one child, by Caesarean section. For some years has been unable to get about at all except in a wheeled chair but she manages to do the cooking and even gardening from her chair. Menstruation began in seventh year. Is the third of a family of five. Others healthy. No history of fractures in family.

On admission, there was gross deformity of legs both above and below the knees. Recent fracture of left tibia—very tender. Sits up straight in bed; spine reasonably normal. Arms and hands functionally excellent. Large pigmented areas on back and left arm. Radiological investigations at eighteen years showed diffuse changes, cystic in places, involving almost the whole of the shafts of the femora, tibiae and fibulae. Pelvis grossly deformed but showed no fibrotic lesions. Films taken at age of thirty four years showed all the major long bones affected in the arms and legs, with the exception of both ulnae and both clavicles. Changes in the legs were far more advanced than in the arms, and included two striking features, marked diminution in calibre of parts of the femoral and tibial shafts and the presence of intensely dense patches in the bones. Changes in the humeri were more advanced than those in the radii. (Latterly under Mr H. L.-C. Wood.)



FIG. 281

Case 90—Femora at eighteen years, showing the diffuse changes in both bones and marked deformity. Note also the gross distortion of the pelvis.

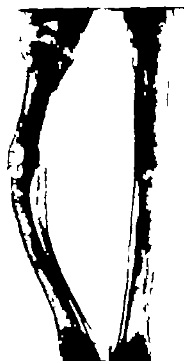


Fig. 282



Fig. 283

Case 90—Figure 282, legs at eighteen years showing the difference in appearance of the tibiae. Both fibulae also show fibrotic changes. Figure 283 right knee and leg at thirty-four years, showing patches of extreme density in all the bones, with variation in calibre and gross deformity of tibia and fibula. Note that the epiphysial parts of femur and tibia are relatively free from changes.



Fig. 284



Fig. 285

Case 90—Figure 284 is a radiograph of the forearms at thirty four years, showing fibrocystic changes in the radii but not in the ulnae. Note that the changes are much less advanced than those in the legs. Figure 285 shows the areas of pigmentation on the left arm and the deformity of the right leg.

CASE 91—POLYOSTOTIC FIBROUS DYSPLASIA (Limited unilateral distribution)

(Figs. 296 to 300.) Female aged nineteen years. Complained of pain and swelling of left ankle for past eighteen months. Minor injury to ankle six months before swelling was noticed. Family history negative. Slight limitation of movement of left ankle, not hot, not tender. Radiographs showed cystic enlargement of left lateral malleolus, and clear cyst-like changes in the inner half of the left tibial head and in the neck of the left humerus. In the tibia and fibula, but not in the humerus, the lesions involved the epiphyses which in both bones were united to the shafts. No changes in the rest of the skeleton including the skull. Serum calcium on two occasions was 10·0 and 11·1 milligrammes per 100 cubic centimetres, but investigation of the calcium excretion suggested mild hyperparathyroidism.

Operation on fibula (H.A.T.F.). Contents of cysts curetted out, cavity cauterised and filled with bone shavings from tibia. Material curetted out was dark red, soft and contained spicules of bone. Sections showed woven bone with all marrow spaces filled with fibrous tissue containing a few minute cysts apparently haemorrhagic in origin. In places there was no fibre bone and the fibrous marrow were dense and contained large numbers of osteoclasts, an unusual finding in the absence of hyperparathyroidism. Professor R. A. Willis kindly examined the section and confirmed the diagnosis. Three weeks after operation the serum calcium rose to 12·7 milligrammes per 100 cubic centimetres, the plasma phosphorus was 3 milligrammes per 100 cubic centimetres. The neck was explored but no parathyroid tumour was discovered. Two months later the serum calcium was 10·4 milligrammes per 100 cubic centimetres, the plasma phosphorus 2·6 milligrammes per 100 cubic centimetres.

Five and a half years later radiographs showed good consolidation of the lower end of the fibula, and reduction in size with surrounding sclerosis of the lesion in the tibia; no appreciable change was seen in the humerus. There was no generalised osteoporosis, and the amounts of calcium and phosphorus in the blood were within normal limits. (Under Mr H. L.-C. Wood.)



FIG. 296

Case 91—Left ankle showing cyst-like changes in the fibula involving the epiphysis as well as the metaphysis.



FIG. 297

Case 91—Left ankle showing consolidation of the cystic area in the fibula, nearly six years after operative treatment.



Fig 288

Case 91—Left humerus showing (*left*) cystic changes at upper end of shaft, and (*right*) the same nearly six years later



Fig. 289

Case 91—Legs showing clear areas in left tibia without distortion of the cortex. Note that the epiphysis is involved.



Fig. 290

Case 91—Section of biopsy specimen from the fibula, showing mass of cellular fibrous tissue and in part of the section a quite unusual number of giant cells. (×50)

LEONTIASIS OSSEA

Synonym—Hyperostosis of Skull

This somewhat rare condition is characterised by hyperostosis of the facial and cranial bones. The name was suggested by Virchow (1864) because the thickening of the skull may produce a leonine appearance similar to that caused by soft tissue swelling (leontiasis) in some cases of leprosy. The literature on the subject is somewhat confusing since apparently identical changes in the skull have been reported under various titles, and Paget's disease may produce somewhat similar changes; individual cases may be labelled differently by different observers. The essential change is diffuse fibrosis combined with new bone formation (hyperostosis). The thickening of the affected facial bones occurs both on the surface and towards the air sinuses, but in the cranial bones the thickening is practically confined to the outer surface. The inner surface of the calvaria may be slightly distorted and wavy but, in most cases, shows little change.

There seems no reason for regarding leontiasis ossea occurring alone as different and distinct from the hyperostosis of the skull seen in many cases of polyostotic fibrous dysplasia. When in this latter condition the distribution of the changes in the limb bones is more or less unilateral, skull thickening if present occurs on the same side. Asymmetry of the face is by no means uncommon in these cases. It may be recalled that the skull is affected in about one-third of the cases of polyostotic fibrous dysplasia without pigmentation and in two-thirds of the cases exhibiting the so-called Albright syndrome. It may be assumed, particularly of the earlier reports, that in many cases of leontiasis ossea the skeleton was never searched for other lesions.

Eden (1939) classified benign fibro-osseous tumours of the skull into four groups, two of which he designated "localised fibrous or spongy osteomas" and "diffuse osteomas or hyperostoses" respectively. Apparently the only real difference between these two types is that in the localised variety the changes are confined to a single bone, and show no tendency to invade adjacent bones, whereas in the diffuse osteomas there is no limit to their spread. His other two groups—ossifying fibroma and compact osteoma—display no resemblance to leontiasis.

There is something to be said for the view that leontiasis ossea should be regarded as a term for a "clinical picture" rather than as a disease or clinical entity.

Knaggs (1923) made an extensive study of the museum specimens and early records in this country and divided the cases of leontiasis into two groups—1) creeping periostitis, and 2) diffuse osteitis. The second group Eden regards as the same as his diffuse osteomas or hyperostoses. Knaggs, while regarding this group as a form of "osteitis fibrosa," emphasized the "complete absence of periosteal bone deposits," yet he added that the bone is enlarged "often enormously, but ... the enlargement gives the impression that the bone is swollen." There is no doubt, however, that in cases of leontiasis which on section show fibrosis there are often local swellings and thickenings which it is difficult to believe are not due to new bone formation on the surface; many of them, even though not so advanced, are in fact strongly suggestive of the cases figured by Knaggs as examples of his first group. Sections of a bone thickened by "creeping periostitis" showed fine-mesh cancellous bone not only in the new subperiosteal bone but also in what had been the original bone. There does not appear to be any account of the soft tissues that filled the spaces in the hyperostotic bone in these cases collected by Knaggs. In one case the hyoid and one fibula were affected; the fibula, which was enormously enlarged, was examined microscopically after death, but no report was given of the contents of the marrow spaces. We have no definite information whether or not diffuse fibrosis was present in these cases.

We are not convinced there is a material difference between Knaggs' two groups, although one is more diffuse and smooth than the other. In his second group he includes four cases in which the whole skull was more or less uniformly thickened, the appearance being strongly

typical of Paget's disease. Only occasionally are clear areas seen suggestive of cystic change and even more rarely are these seen on the surface looking like blisters. The frontal and other sinuses are usually invisible. As already stated in most cases the outer table is chiefly affected, the inner showing little if any change. Windholz (1945) reported the case of a woman of sixty three years with what he considered to be signs of both osteoporosis circumscripta and leontiasis; the fibrotic changes characteristic of the latter condition were confirmed by biopsy.

Progress.—As a rule the condition is slowly progressive for many years. A history extending over forty-six years was reported by Kirkland (1941). Growth may be arrested ultimately; when the onset has been early it may cease to extend when skeletal growth ceases (Eden 1939). As in the other skeletal lesions that occur in polyostotic fibrous dysplasia, growth may be dormant for years. In a boy with the whole skull thickened, and changes in other bones, films taken after an interval of three and a half years showed definite increase in the thickening of the inner table while in the outer table there was little if any further change, a reversal of the usual course followed by the hyperostosis (Gemmell 1935).

Pathology.—Sections reveal fine-mesh cancellous spongy bone both forming the hyperostosis and replacing the bone beneath it, but as a rule leaving unchanged the inner table of the skull. All the spaces in the cancellous bone are filled with cellular fibrous tissue. Signs of active absorption of old bone and replacement by new, largely of the woven type, are usually to be seen. Calcium spheroids may be present in the fibrous tissue (Eden 1939). There is not the same tendency to a mosaic arrangement of the new bone as in Paget's disease.

Complications.—Malignant change has been reported once only, a fibro-sarcoma growing in the naso-pharynx of a patient with generalised thickening of the skull, which had been present for at least seven years (Stack 1900). Kirkland reported a man of fifty four with grotesque deformity of the head, who in addition to kypho-scoliosis had multiple rodent ulcers.

Diagnosis.—Paget's disease is the most frequent alternative diagnosis. In this disease the skull is more likely to be diffusely and smoothly thickened, whereas in leontiasis the thickening is usually more localised and protuberant. Leontiasis typically affects the facial bones though the cranium is by no means exempt, whereas in Paget's disease the cranium is the site of election, the facial bones being invaded only in exceptional cases—in not more than 8 or 9 per cent (Eden 1939). In Paget's disease the skull is more coarsely mottled with larger woolly dense spots. The age of the patient may be an important or decisive factor, while the nature of any changes present elsewhere in the skeleton should point strongly to the correct diagnosis.

The presence of pigmentation and a history of precocious puberty in Albright's syndrome would also be decisive. Meningiomas may cause local hyperostosis, asymmetry of the face and exophthalmos (Rowbotham 1939). Hyperostosis frontalis interna, which occurs almost exclusively in females and is associated with obesity and a variety of cerebral disturbances, should not be difficult to distinguish since it is the inner table of the skull alone that is thickened, the very part that is usually unaffected in leontiasis.

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CHAPTER 22

HYPERPARATHYROIDISM

Osteitis Fibrosa Generalisata (von Recklinghausen)

Primary hyperparathyroidism which has produced changes in the bones is characterised by generalised decalcification of the skeleton associated with fibrocystic bone lesions and osteoclastomata hypercalcaemia and excessive excretion of calcium and phosphorus in the urine In many cases bilateral lithiasis is also present Typical bone changes with or without renal complications, were present in nearly 40 per cent of sixty three consecutive cases of hyperparathyroidism treated at the Mayo Clinic, all confirmed by operation on the neck (Black 1948) In at least a further 20 per cent there was some osteoporosis in addition to renal lithiasis, but without fibrocystic bone changes In 35 per cent, there were renal effects only with no changes in the bones. Secondary or compensatory hyperplasia of the parathyroids may also occur in certain affections of the skeleton namely in osteomalacia, rickets, chronic renal failure with acidosis especially in children and adolescents in whom either renal rickets or simple osteoporosis has developed, and very rarely in multiple myelomata and generalised malignant disease Some enlargement of the parathyroid glands has been found in acromegaly and even in a few severe cases of polyostotic fibrous dysplasia but without generalised osteoporosis. Von Recklinghausen reported his first case in 1891 Valuable reviews of hyperparathyroidism have been published by Hunter (1937) and Snapper (1940)

Hereditary and familial influences play no part in hyperparathyroidism.

Sex—Females are affected at least twice as frequently as males.

Age—In contrast to polyostotic fibrous dysplasia it principally affects adults of various ages the women being rather older than the men Children are occasionally affected but much less commonly Hadfield and Garrod (1938) found the average age thirty-eight years for males and forty-eight for women.

Etiology—The cause is entirely unknown. In cases in which there is hyperplasia of all the parathyroid glands instead of the more usual tumour of one it has been suggested this is possibly the result of increased secretion of the appropriate hormone by the pituitary (Hunter 1937)

Distribution of the bone changes—The osteoporosis which is such an important feature affects the whole skeleton including the skull. The fibrocystic changes which are secondary may be found in any bone but are seen most often in the limb bones and the pelvis. Less common sites are the vertebrae carpus tarsus and mandible the last mentioned bone has even been the only site of fibrocystic changes though a large parathyroid tumour was present The osteoclastomata are said to occur particularly towards the ends of the long bones, and in the jaws occasionally they have been found in the skull.

Signs and symptoms—A frequent early sign is *pain* which is much commoner and more severe than in polyostotic fibrous dysplasia. The pain is felt in the bones particularly in the legs pelvis and back and may be accompanied by stiffness. The bones are tender and in places may be soft enough to be dented by the fingers. Local symptoms may be relieved by operation on the affected part of a bone *Deformities* resulting from swelling bending or fracture of one or more bones and accompanied by some shortening if a limb is affected, are frequently present particularly if a case is allowed to progress unduly long before the cause is recognised *The parts affected* are the ribs spine and limbs particularly the legs. Walking may become impossible the bones being incapable of supporting the weight of the body The terminal phalanges of the fingers may become shorter and broader than normal—a characteristic deformity The symptoms are by no means confined to the skeleton.

Anorexia sometimes with nausea vomiting and abdominal cramps polydipsia and polyuria all occur and may appear early in a case before the bones show any changes (Hunter 1037) Amenorrhoea may be complained of There may be muscular hypotonia, but this is masked by the bone tenderness or fractures. Patients suffer from fatigue and feel weak and ill. Wasting supervenes as the condition progresses. *Renal complications* are present in one-half to two-thirds of the cases with skeletal changes with or without renal pain and haematuria. Bilateral lithiasis is particularly significant and should raise suspicions of the nature of the case. Sometimes metastatic calcification is found in the kidneys this or superimposed pyelitis may lead to renal failure. In every case in which hyperparathyroidism is suspected from the skeletal changes the urinary tract should be radiographed and the renal function investigated. The signs and symptoms are so varied it is not surprising that the true nature of a case is often not suspected for a considerable time. Examination of the neck reveals a palpable tumour only in a small percentage of the cases, even when a tumour of considerable size is found at operation

Blood examination—Hypercalcaemia and lowered plasma phosphorus are the rule to which there are few exceptions and are of the greatest diagnostic value. The serum calcium exceeds 12 and may be as high as 23 or even 30 milligrams per cent. The inorganic phosphorus is low 1 3 to 3 milligrams per cent unless renal failure is imminent when the plasma phosphorus will rise The alkaline phosphatase is always high when the bones are affected, even as much as twenty times the normal but this is found in so many conditions it is of little value. There is excess of both calcium and phosphorus in the urine. Investigations of the calcium metabolism show a negative balance.

The rapid return to normal of the amounts of calcium and phosphorus in the blood after successful removal of a parathyroid tumour is a welcome confirmation of the accuracy of the diagnosis.

Radiological appearances—The most important change invariably present if the bones are affected at all is generalised osteoporosis of the whole skeleton. This may be the only bone change present, even in an advanced case. In place of the normal contrasting densities of the cortex and medulla, there is a more uniform low density a foggy finely mottled or worm-eaten appearance, except where cysts are present. Changes other than general osteoporosis develop later in the shafts of the major long bones, and these tend to be more local and much less diffuse than those usually seen in polyostotic fibrous dysplasia. The widespread enlargement of a shaft, with a thin cortex and more or less uniform density of the medullary cavity an appearance so common in the non-parathyroid cases may occur but is much less frequently seen in the condition here considered except in the later stages. A ground-glass appearance may however be seen without the considerable enlargement of the bone so common in polyostotic fibrous dysplasia. Much more common is irregular cystic formation with local expansion of the bone An endosteal cyst may however occur with no alteration in the contour of the bone. Sometimes cysts occur *in* the cortex or under the periosteum. The shaft of a bone may be more slender than normal as well as less dense and possess the thinnest possible cortex In advanced cases the density may be so low the bones cast but little shadow on an X-ray film. The pelvis may be indented by pressure from the femora, and is sometimes grossly deformed. In the hands the osteoporosis is particularly well seen the cortices are irregular and the cancellous tufts of the terminal phalanges are almost completely decalcified (Brailsford 1044) In the spine the osteoporotic vertebral bodies are biconcave with the discs deep and biconvex.

To sum up all types of fibrocystic change may occur in both groups of cases. It is the generalised osteoporosis which is the chief distinguishing radiological feature of hyperparathyroidism In the skull the changes show an even greater difference. Instead of the changes being limited in extent at least in the earlier stages and accompanied by

definite local thickening and irregular increase in density of the bone they are more general, with a tendency towards decreased density The whole of the calvaria is fuzzy or very finely mottled and granular there may be some general thickening but it is usually slight the outer table may be fluffy in appearance Here and there may be a clear cystic area.

In some cases metastatic calcification may be seen in the lungs stomach and myocardium as well as in the kidneys. Renal calculi should always be sought for Keynes and Taylor (1933) reported a case with calcification in the synovial membrane and extensor tendon of one knee joint this case developed brilliantly blue sclerotics after having had a variety of symptoms for some years.

Progress—In the undiagnosed case the condition is slowly progressive the bone changes and deformities becoming gradually accentuated the patient becomes weaker and worn out with pain she may become completely crippled and eventually die. If the neck is explored and an enlarged parathyroid is found and removed, improvement takes place rapidly Within a day or two pain and tenderness are reduced or disappear and the patient feels better in every way The bones slowly recalcify the cystic spaces are diminished in size and show signs of becoming obliterated. Failure of the skeleton to recalcify after removal of a parathyroid adenoma has however been reported (Voltz and Smull 1944) Other symptoms present diminish in severity and soon disappear The serum calcium and plasma phosphorus quickly return to normal levels, but the phosphatase remains high. The abnormal excretion of calcium and phosphorus disappears. It is of interest to note that in cases in which the parathyroid tumour has proved to be malignant and its removal has been followed by general improvement the appearance of local recurrences or metastases may be followed by a recurrence of the signs of hyperparathyroidism (Snapper 1949) In one case recurrence of the tumour and return of the hyperparathyroidism occurred no less than four times (De Wesselow and De Wardener 1949)

Complications—The renal complications have been referred to already as they so often form part of the clinical picture and not uncommonly an important part. In one case in which an enlarged parathyroid was actually found at operation, signs of neurofibromatosis were present in addition to fibrocystic changes in some of the bones, apparently a combination of the two diseases described by von Recklinghausen (Cohen and Douady 1936)

Pathology—A hyperfunctioning parathyroid adenoma is found in one occasionally in two of the glands. The tumour usually consists of "principal cells which may be larger than normal with the nuclei hyperchromatic. A few eosinophile cells and giant cells may be scattered throughout the tumour If there is general enlargement of all four glands this is due to excess of abnormally large water-clear cells only (Snapper 1949) An adenoma consisting essentially of water-clear cells or eosinophiles respectively is quite exceptional. Very rarely has the tumour proved to be malignant In secondary hyperplasia either the principal cells or the water-clear cells are chiefly affected.

The bones when severely affected are soft and cut like "rotten wood. On section are seen grey gelatinous masses containing gritty bone brown or reddish tumours and cysts. The brown tumours contain derivatives of haemoglobin. The cysts lined by fibrous tissue may have membranous partitions crossing them occasionally a cyst is surrounded by smooth bone with no fibrous lining (Elmslie *et al* 1933) The histological changes have been fully discussed by Turnbull (Hunter and Turnbull 1931) and by Hadfield and Garrod (1938) They consist of lacunar absorption apposition fibrosis of the marrow and formation of osteoclastomata and cysts. Fibrosis of the marrow is widespread but not universal. Cysts are common particularly in the larger areas of fibrosis. The compact bone is replaced by spongy There is no excess of osteoid, i.e there is no delay in calcification. The new bone is largely woven bone There is much less tendency to a fine mosaic arrangement than in Paget s disease In hyperparathyroidism the new bone is removed by osteoclasts almost as soon as

it is formed whereas in Paget's disease resorption and apposition are more evenly balanced. The osteoclastomata vary in size from a collection of a few giant cells to a large tumour. The giant cells may contain red cells and haemosiderin.

Diagnosis—From polyostotic fibrous dysplasia the diagnosis depends chiefly on the presence of generalised osteoporosis in addition to local changes in the bones, hypercalcaemia with low inorganic phosphorus and excessive excretion in the urine of both calcium and phosphorus. Pain is a much more prominent feature in hyperparathyroidism. Areas of pigmentation and precocious puberty do not occur in this condition as they may with polyostotic fibrous dysplasia.

Paget's disease though it may be widespread, is never completely generalised and is readily distinguished in most cases. As a rule the honeycombing of the long bones affected with fibrosis in Paget's disease is combined with definite new bone formation on the surface the new bone also being honeycombed the cortex is not distended from within and thinned as in hyperparathyroidism. The changes in the skull also differ considerably. In Paget's disease the calvaria displays irregular increase in density and is thickened, whereas in hyperparathyroidism it is decalcified and mottled with little if any thickening. Though the alkaline phosphatase in the blood is raised in both conditions, there is no hypercalcaemia in Paget's disease. The younger the patient the more likely is the case to be one of hyperparathyroidism.

In multiple myeloma the plasma phosphatase is normal in amount or only slightly raised while in most cases there is no hypercalcaemia and the plasma phosphorus is normal. Occasionally the serum calcium is increased considerably. Bence-Jones protein is often found in the urine hyperproteinaemia and increase of globulins are common. The radiographic picture particularly of the skull is usually distinctive in spite of there often being some generalised decalcification of the skeleton. The multiple clear lesions are sharply outlined and are often numerous. Sternal puncture may give decisive results.

From widespread carcinomatosis diagnosis is occasionally difficult for instance when no primary tumour is discovered and the general decalcification is marked. The serum calcium may be high and the excretion of calcium increased while the appearance of the skull may be similar in the two conditions. Secondary hyperplasia of the parathyroids has even occurred in carcinomatosis (Snapper 1949).

In osteomalacia both the calcium and phosphorus in the blood are low. In xanthomatosis there is no general decalcification and no corresponding blood changes. Sternal puncture may be helpful in Gaucher's disease. Osteoporosis sufficiently marked to be of clinical importance is distinctly rare in xanthomatosis. The diagnosis should be easy.

Renal calculi particularly if bilateral would be a strong point against any of these alternative diagnoses. In cases of renal osteo-dystrophy with osteoporosis in both children and adults though secondary hyperplasia of the parathyroids may be present the serum calcium is usually reduced or at least relatively low while the plasma phosphorus is markedly raised. Fanconi's syndrome a condition very seldom met with particularly in adults may be distinguished by the presence of renal glycosuria. True diabetes mellitus is also a possible cause of generalised osteoporosis which may result from the long continued acidosis (Lawrence 1948).

Thyrotoxic osteoporosis should be recognised without difficulty. Tenderness of the bones may be present. Diffuse fibrosis of bone has been reported as a complication of this type of general osteoporosis (Jaffe *et al.* 1932. Askanazy and Rutishauser 1933). The generalised osteoporosis of Cushing's pituitary basophilism is accompanied by "plethoric adiposity" hypertrichosis and amenorrhoea in females (who are much more commonly affected than males) vascular hypertension acrocyanosis and, quite commonly hyperglycaemia. Young adults and occasionally young girls are affected. There is no hypercalcaemia. Finally simple senile osteoporosis without definite cause must not be forgotten. In this the spine is particularly affected and crush fractures of vertebral bodies are common.

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CASE 92—HYPERPARATHYROIDISM

(Figs. 201 to 206.) J. L. male aged eight years. Admitted with three months history following tonsillitis of anorexia, increasing polydipsia and enuresis pains in the head abdomen and knees and occasional vomiting. Later complained of stiffness of neck and frontal headache. So weak he was unable to walk. Family history negative. B.S.R. 47 millimetres in one hour. Urine albumin. Blood urea normal. X rays revealed nothing abnormal. Symptoms continued for five months. Polydipsia marked. Pains increased. Tenderness of back and limbs developed. B.S.R. 60 millimetres in one hour. Various laboratory investigations negative. Normal ventriculogram performed. Biopsy of skull showed marked osteoporosis. Radiographs now showed generalised osteoporosis of the whole skeleton. The skull showed typical fine mottling. There were no very definite cysts, but films of the hips and knees showed unusual features—symmetrical erosive lesions of the cortex on the inner side of the necks of the femora and on the inner side of the tibiae just below the heads. Serum calcium 18·8 milligrams per 100 cubic centimetres, plasma phosphorus 2·8 milligrams per 100 cubic centimetres alkaline phosphatase 93 units.

Neck explored parathyroid tumour removed from behind sternal notch by Mr C. Donald. Immediate improvement followed—anorexia, pains and stiffness soon disappeared. Enuresis stopped. Serum calcium fell to 8·9 milligrams per 100 cubic centimetres in forty-eight hours and to 6·5 milligrams per 100 cubic centimetres in a week. Alkaline phosphatase remained high, 107, 87 and 92 units on three occasions. B.S.R. also remained raised. Gained over four pounds in weight in three weeks. The recalcification of the skeleton proceeded steadily and was eventually satisfactory. The cortical lesions on the inner side of the necks of the femora and on the tibiae were no longer visible in films taken four months after operation.

Section of the parathyroid tumour showed transitional principal cells predominating, with many giant nuclei present.

(Under Dr W. G. Wyllie. Reported by Dr R. J. Pugh. Proceedings of the Royal Society of Medicine 1946 39 604.)



FIG. 201

Case 92—Skull showing general decalcification with fine mottling, and flatness of the outer table

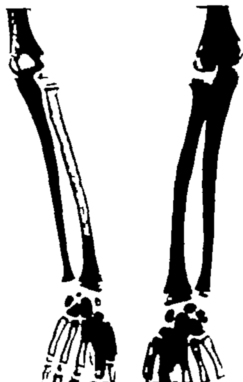


Fig. 292



Fig. 293

Case 92 Fig. 292—Left forearm, with right forearm of control for comparison, showing the general osteoporosis of the bones. Fig. 293—Pelvis and femora showing general osteoporosis and *symmetrical erosion on the inner side of necks of both femora, particularly the left.*

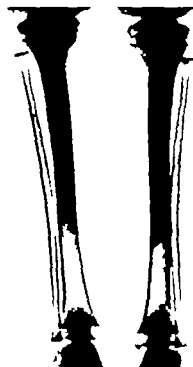


Fig. 294

Case 9[illegible]—Legs showing the symmetrical cortical erosion on the inner side of the tibiae just below the head. The osteoporosis is not well seen in this film.

CASE 92—HYPERPARATHYROIDISM

(Figs. 291 to 296) J. L. male aged eight years. Admitted with three months history following tonsillitis of anorexia, increasing polydipsia and enuresis pains in the head, abdomen and knees and occasional vomiting. Later complained of stiffness of neck and frontal headache. So weak he was unable to walk. Family history negative. B.S.R. 47 millimetres in one hour. Urine albumin. Blood urea normal. X-rays revealed nothing abnormal. Symptoms continued for five months. Polydipsia marked. Pains increased. Tenderness of back and limbs developed. B.S.R. 60 millimetres in one hour. Various laboratory investigations negative. Normal ventriculogram performed. Biopsy of skull showed marked osteoporosis. Radiographs now showed generalised osteoporosis of the whole skeleton. The skull showed typical fine mottling. There were no very definite cysts, but films of the hips and knees showed unusual features—symmetrical erosive lesions of the cortex on the inner side of the necks of the femora and on the inner side of the tibiae just below the heads. Serum calcium 18·8 milligrams per 100 cubic centimetres, plasma phosphorus 2·8 milligrams per 100 cubic centimetres alkaline phosphatase 03 units.

Neck explored parathyroid tumour removed from behind sternal notch by Mr C. Donald. Immediate improvement followed—anorexia, pains and stiffness soon disappeared. Enuresis stopped. Serum calcium fell to 8·9 milligrams per 100 cubic centimetres in forty-eight hours and to 6·3 milligrams per 100 cubic centimetres in a week. Alkaline phosphatase remained high 107 87 and 62 units on three occasions. B.S.R. also remained raised. Gained over four pounds in weight in three weeks. The recalcification of the skeleton proceeded steadily and was eventually satisfactory. The cortical lesions on the inner side of the necks of the femora and on the tibiae were no longer visible in films taken four months after operation.

Section of the parathyroid tumour showed transitional principal cells predominating, with many giant nuclei present.

(Under Dr W. G. Wyllie. Reported by Dr R. J. Pugh. Proceedings of the Royal Society of Medicine 1946 39 694.)



FIG. 291

Case 92. Skull showing general decalcification with fine mottling, and thinness of the outer table.

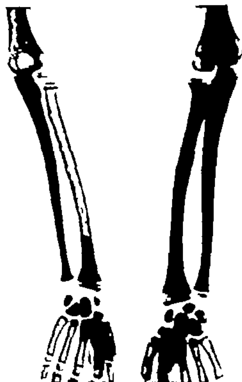


FIG 292



FIG 293

Case 92. Fig 292—Left forearm, with right forearm of control for comparison, showing the general osteoporosis of the bones. Fig. 293—Pelvis and femora showing general osteoporosis and symmetrical erosion on the inner side of necks of both femora, particularly the left.



FIG 294

Case 92 —Legs showing the symmetrical cortical erosions on the inner side of the tibiae just below the head The osteoporosis is not well seen in this film.



FIG 295

Case 92—Pelvis and femora four months after removal of parathyroid tumour Note the marked improvement in the density of the bones and disappearance of the cortical lesions on the inner side of the femora.

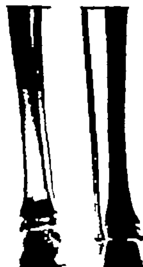


FIG. 296

Case 92—Posterior view of right leg with control (on right) six months after removal of the parathyroid tumour showing the density of the bones is still subnormal.

CASE 93—HYPERPARATHYROIDISM

(Figs. 297 to 301.) S D girl aged fourteen years. Two years ago genu valgum was noticed and treated by osteotomy has been unable to walk since Later radiographs showed generalised osteoporosis with little sign of cystic change bilateral coxa vara and deformity of the humeral necks the appearance was suggestive of renal rickets. Serum calcium 16·6 milligrams and plasma phosphorus 2·8 milligrams per 100 cubic centimetres. Alkaline phosphatase 30 units Estimations on two occasions showed gross excess of calcium in the urine No signs of renal disease Neck explored and parathyroid tumour removed by Mr R. Maingot (January 1930) Patient made a good recovery but recalcification was rather slow The negative calcium balance became positive Serum calcium 10·0 milligrams plasma phosphorus 6 milligrams per 100 cubic centimetres. Alkaline phosphatase 37 units.

Two and a half years after operation the skeleton generally was of normal density there was still a suspicion of cystic change in the shafts of the tibiae (Under Mr St J D Buxton.)



Case 9 hips in Novemb g general ll the bones at par ently the al slipping of l



FIG. 298
Case 93—Thorax and shoulders in November 1938, showing the poor calcification of all the bones and the deformity of the humeral necks.



FIG. 299
Case 93—Hips in August 1941 showing the bones now well calcified, but the coxa vara deformity still present.



FIG. 300
Case 93—Left shoulder in August 1941 showing the normal calcification of the bones, and the deformity of the upper end of the humerus.



FIG. 301
Case 93—Lateral views of the legs August 1941 showing the remains of cystic changes in the tibiae still visible.

CHAPTER 23

PAGET'S DISEASE

Synonym—Osteitis Deformans

This chronic disease is characterised by slowly spreading changes in one or more bones, the changes consisting of decalcification coupled with hyperostosis and with the marrow spaces in the transformed bone occupied, partially or completely by vascular fibrous tissue Czerny (1873) suggested the name osteitis deformans, but ever since the publication in 1877 of Paget's paper in which he described with characteristic lucidity the clinical features of eight cases his name has been coupled universally with the disease. In 1908 Elmslie collected ninety cases and reviewed the whole subject, and in 1938 Brailsford discussed the changes in 154 cases which he had examined radiologically

Hereditary and familial influences are evident in some cases. In seven of Elmslie's ninety cases other members of the family were affected. Since that date many instances have been recorded in parents and offspring and in brothers and sisters. We have twice met with two brothers afflicted with this disease.

Age—The majority of cases are seen between fifty and seventy years of age. Though uncommon before the age of forty several unquestionable cases have been diagnosed at thirty years. Since in some of these more than one bone was affected, the disease was unlikely to have been a recent development.

Sex—Males are rather more commonly affected than females.

Incidence—Paget's disease is one of the obscure diseases of the skeleton which are relatively common many cases being discovered incidentally when investigated radiologically for symptoms entirely unconnected with the bone condition. Incidence figures most likely to approach accuracy are obtainable only from radiological departments. Inquiry some ten years ago from the radiologists of the teaching hospitals of London revealed that the average annual number of Paget cases seen at each hospital was approximately fifty

Distribution—The disease may be confined to one bone, at least for a period of years. The tibia is a common site for a solitary lesion. Sooner or later in most cases several bones are affected only exceptionally is the disease so widespread as to be almost generalised. Published lists of the bones most commonly affected in order of frequency vary but they all agree in placing the pelvis at the head of the list It showed changes in 243 cases out of a total of 367 reviewed by Dickson *et al* (1945) The femur tibia lower spine and skull are all common sites. The humerus clavicle and forearm bones are distinctly less common, while the hand and foot with the possible exception of the tarsal bones are seldom affected a point in which the disease differs from polyostotic fibrous dysplasia. The ribs and the manubrium sterni—occasionally even the whole of the sternum—may be affected. When the skull is involved the facial bones very seldom show changes, an important point of difference from leontiasis ossea In the tibia the changes spread from the upper end far more commonly than from the lower the same is true of the femur Changes may begin at both ends of a bone but this is excessively uncommon

The distribution appears to be almost entirely erratic, and shows little if any tendency to be symmetrical. When however the pelvis is involved there is a greater chance than otherwise of finding the upper end of one or both femora and the sacrum and lower spine also showing changes.

Etiology—The cause is unknown. The inflammatory hypothesis, making infection responsible, is now generally discarded. There is no endocrine error the parathyroid glands are normal and their removal in this disease is useless and unjustifiable Disorder of mineral metabolism is suggested as the possible cause (Hunter 1948) Injury has been suspected of playing a part in the incidence of the disease in a few cases. In one patient a man of thirty-seven years with typical Paget changes in a tibia, swelling of this bone had been present ever since an injury at the age of fourteen years.

Signs and symptoms—Though it is agreed that the changes in one or more bones are often no more than an incidental finding there is considerable variation in the percentage said to have symptoms referable to the osseous lesions. Only 48 per cent. of eighty two cases studied by Newman (1946) have symptoms closely related to the Paget's disease. He found that only 35 per cent. complained of pain whereas Hunter (1948) stated that pain usually in the back of the legs, was present in as many as 80 per cent. We find difficulty in accepting the latter figure if the cases discovered incidentally by the radiologists are included. The pain is of various types, occurs at various times of the day or night and is provoked by a variety of causes. For instance pain in a tibia may be worse in bed, or on walking may be concentrated at the limit of the changes in the bones. Headache is common and may be caused or exaggerated by exercise or coughing Kay *et al* (1934) found headache severe in eight of thirty four cases. Spontaneous diminution or complete disappearance of pain may occur Dickson *et al* (1945) found backache in 119 cases, headache in sixty four and pain in the legs in fifty-eight of the 367 cases studied by them. Swelling and deformity may call attention to the disease when a tibia is involved, and increase in size of the head (necessitating repeated purchase of larger hats) is a frequent cause of complaint when the skull is affected. In a tibial case the overlying skin is often warmer than that on the other side, and occasionally it is even red or oedematous, but only quite exceptionally is tenderness present. An affected tibia is thickened its anterior margin rounded, and the deformity further increased by antero-lateral bowing Thickening of other affected bones and increase of their normal curves may be readily felt. When the upper part of the femur is affected signs of coxa vara may be present. Limitation of abduction at the hips may however be due to deepening of the socket or osteoarthritis in addition to coxa vara. In an advanced case, with many bones affected the crouching or "simian" attitude assumed on standing may be suggestive The large head is held low with the chin thrust forwards, the chest is flattened laterally the spine is kyphotic and the legs are bowed antero-laterally with the joints slightly flexed. The reduction in stature resulting from deformities may be considerable in one case (Osler quoted by Lewin 1922) the reduction amounted to thirteen inches, and even this was exceeded in a case reported by Hurwitz (1913) Though as a rule the curvature of a bone results in approximation of the ends, apparently authentic cases of lengthening have been observed Elmslie (1908) stated that "numerous instances had been recorded. We have seen a tibia which was three-quarters of an inch longer than the opposite normal bone. Another convincing case with an elongated radius curving round a normal ulna, was published by Vilvandré (Kay *et al* 1934) Fixed pronation deformity produced in this way was first called attention to by Symonds (1881) Fracture may be the initial occurrence the bones most often affected being the femur and tibia Deafness due to otosclerosis—not to pressure on the auditory nerve—is common but only in those with the skull obviously affected (Jenkins 1923) Interference with vision, by pressure on the optic nerve occurs much less often Arterial degeneration is common in the older cases, often with retinal haemorrhages and choroidal changes Calcareous arteries are frequently found—in as many as 40 per cent. of the cases according to Hunter (1948) We are inclined to doubt the statement that Paget's disease occurs with special frequency in those exhibiting premature senility

Blood examination—The only constant change is the increase often to as much as twenty or thirty times the normal, of the alkaline phosphatase the amount varying roughly with the

severity of the disease. The acid phosphatase is increased only quite exceptionally. The serum calcium is normal in amount and so may be the plasma phosphorus, but this is often high. The excretion of calcium and phosphorus is increased but the amounts have no relation to the severity of a case. Since the kidneys are taxed, hypercalcaemia may occur late in the course of the disease. Increase in the proportion of basophil and eosinophil cells is reported by Pines (1935). Glycosuria is present in some cases, the pituitary being suspected as possibly responsible.

Radiographic appearances—Excluding the skull, the changes in the bones may be divided into four types: 1) honeycombed or spongy, 2) striated, 3) dense, and 4) grossly cystic. Two or more of these may be found in a case or even in a single bone. In the tibia, for instance, during the early years of the disease when it is slowly spreading, it is common to find a clear cyst-like appearance at the advancing point and honeycombed changes behind it. Generally speaking the honeycombed appearance is the commonest and most widespread. The next most common type is the striated, in which the trabeculations, standing out boldly, show a greater inclination to be parallel than those in the honeycombed type. Striation may be seen in any bone but more often, perhaps, in the pelvis, sacrum, vertebral bodies and calcaneum. Thurstan Holland (1923) called attention to the appearance of striation in the calcaneum while the bone was still apparently unaffected by the disease, and he regarded it as an early sign of some diagnostic value. The dense type is seen typically in the spine in some cases, the bodies of certain vertebrae showing uniform increased density with little if any increase in size. If two or more vertebrae are affected they are not necessarily adjacent. It is a curious fact that if a vertebral body is dense it is as a rule uniformly dense throughout. Apart from the advancing point of the disease seen typically in the tibia, as already mentioned, a grossly cystic appearance is uncommon; we have met with it in the fibula, the diagnosis being *impossible until typical Paget changes were discovered in the opposite tibia and other bones.* We have seen it also in the radius. Clear areas worthy of being called cystic are occasionally seen in the pelvis. Though there seems to be a preference in some cases for one particular type of change, there is general agreement that in most cases there is a tendency for affected bones to become denser in the course of time. The primary changes in the shaft of a long bone are essentially *in* the cortex, which appears to be partly or completely decalcified; new bone is formed both on the surface under the periosteum and towards the medulla, and later replaces, to a varying extent, the decalcified cortex. The diagnostic value of the pointed extremity of the changes in the shaft of a long bone has been appreciated for many years, attention being called to it, we believe, by the late Professor S. G. Shattock. The ends of the long bones are less commonly affected than the shafts, but coarse trabeculation, for instance *of a femoral condyle, may be the first sign of disease in the bone. In the pelvis* the essential change may be increase in the density of the bone, but in our experience this is much less common than honeycombing. The pelvis may be indented, but this is also exceptional.

In the skull there is thickening of the outer table and irregular increased density. In a typical case the calvaria is considerably thickened, with the surface somewhat ill-defined, and the bones coarsely mottled with dense rounded "cotton wool" spots of varying size. The sutures are obliterated. The changes are more likely to be generalised throughout the calvaria than in leontiasis, and are much less likely to involve the maxillae. In some cases clear areas are seen, and these may be sufficiently marked to warrant the title of *osteoporosis circumscripta cranii.* Of forty-seven cases of this latter condition, thirty-two had Paget's disease in addition, and in eighteen of these both conditions were present in the skull (Kasabach and Gutman, 1937). These authors suggested there was justification for regarding osteoporosis circumscripta as either an atypical form of Paget's disease or a precursor of it. There is no general agreement, however, as to the cause and nature of osteoporosis circumscripta; possibly it should be regarded as a clinical feature rather than as a clinical entity. Windholz (194) suggests that it results from circulatory disturbance at the base of the skull caused by a variety of conditions.

There is no constant change in the pituitary fossa. The pineal gland may be calcified (Brailsford 1938)

The normal curve of an affected long bone is increased and the deformity is accentuated by thickening on the convex side of the curve. Coxa vara may occur but this is often more apparent than real, the deformity as a rule occurring in the shaft of the bone. Arthritic lipping of the vertebral bodies is naturally common at the age at which Paget's disease is most frequently seen. According to Snapper (1949) the Paget changes begin in the lipping and spread to the body.

Fractures, if present, are abrupt, more or less transverse and are seldom comminuted. Decalcification of the fragments in the region of the fracture may be so rapid and coarse that the presence of a malignant growth may be suspected. Multiple partial fractures are occasionally seen on the convex side of a curved bone (see below). Collapse of a vertebral body may occur but is uncommon.

Progress—In an individual long bone the changes steadily progress till the whole shaft is involved. Deformities also steadily increase for a time but not indefinitely. The skull when affected gradually increases in size. Low diastolic pressure and cardiac failure are not infrequent in the later stages.

Complications—Fractures are not uncommon, and may occur with greater ease than normal but it is doubtful whether they occur with much greater frequency than is usual in those of advanced age. Common sites are the upper third of the femoral shaft and the tibia a little below the head. Less common sites are the humerus, lower third of tibia, patella and pelvis. Pain after a fracture may be less than usual. Union takes place readily but a fracture in the upper third of the tibia, often a horizontal crack with no displacement, produces minimal callus and may be slow in disappearing. Incomplete fractures sometimes occur and several may be seen in a single bone but only in quite exceptional cases (Roberts and Cohen 1923, Allen and John 1937, Brailsford 1938, Dickson *et al* 1945). The femur and tibia are the bones affected in this way, healing takes place with a minimum of callus. A partial fracture may become complete. Paraplegia due to hyperostosis of one or more vertebrae is very uncommon but certainly occurs. Urinary calculus was present in twenty two of 367 cases (Dickson *et al* 1945)

Sarcoma is a well-known complication of an advanced case but we believe that the incidence has often been much exaggerated since the days of Paget. The frequency has been variously given as .4 per cent (Newman 1946) up to 11 per cent. (Bird 1927). Dickson *et al*, however, in their 367 cases found only three with sarcoma. Inquiry in 1938 from a dozen leading radiologists in London, many of whom were seeing a fresh case of Paget's disease almost every week, revealed that the number of cases with sarcoma seen by any single man in his life varied from one to five. There was one exception, a radiologist concerned, we believe, more with therapy than diagnosis, who regarded sarcomas as by no means a rarity. The fact that Platt (1947) had dealt with twelve cases of sarcoma occurring in Paget bones should be regarded as an indication of his reputation for exceptional knowledge and experience of bone tumours rather than as a true indication of the frequency of this complication. One of Platt's cases had multiple tumours of the skull, other similar cases have been reported. In patients over fifty years of age with sarcoma of the bone a considerable proportion—28 per cent, according to Coley and Sharp (1931)—have Paget's disease in addition, both affecting the same bone. This complication is distinctly more common in males, and is seen most often when they are approaching the age of sixty, whereas the average age of all bone sarcomas is twenty three years (Bird 1927). The new growth occurs only in a bone showing Paget changes, usually in a lesion of the osteolytic rather than the sclerotic type (Sear 1949). The simultaneous occurrence of sarcoma in more than one bone has been reported in several cases (Albertini 1928, Gerstel and Janker 1933, Davie and Cooke 1937). Of seventy-six collected cases of sarcoma complicating Paget's disease, twenty-six showed multiple bone involvement



Fig. 302



Fig. 303

Case 94—Figure 302, skull showing gross increase in thickness—one and five-eighths inches [illegible] an unreduced radiograph—of whole calvaria, but not of base. Fairly typical mottling. Figure 303, right arm showing honeycombed type of disease in humerus and ulna and some atypical change in the radius.



Fig. 304

Case 94—Left side of pelvis and femur showing advanced changes of mixed honeycombed and striated types, and marked bowing of femur

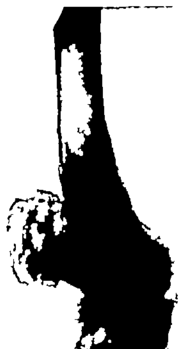


Fig. 305

Case 94—Knee joint showing typical changes in all three bones

CASE 95—PAGET'S DISEASE

(Figs. 306 and 307) Male aged sixty five years. Had rickets in infancy Fifteen years ago noticed hats were small after a year's wear Head stopped growing two years ago Has lost two and a half inches in height General health good. Head large and lumpy on top Right clavicle enlarged and right iliac crest thickened. Kypho-scoliosis rather marked, with reduction of mobility Considerable limitation of movement of hips except flexion. Slight general bowing of legs no obvious thickening Skull pelvis and lower spine show typical changes. Left tibia shows very early disease below the tubercle Pelvis is deformed. Diagnosed as Paget's disease five years ago

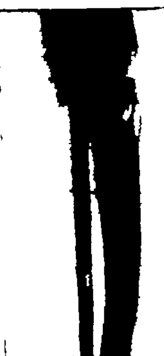




FIG. 306 FIG. 307

Case 95—Figure 306 left tibia showing very early Paget changes in the region of the tubercle. Note the area of decalcification with a pointed lower extremity in the anterior cortex. Figure 307 pelvis and upper femora show Paget changes of various types including increased density Note pelvis is deformed.

CASE 96—PAGET'S DISEASE

(Fig 308) Male aged forty two years. Complained of pain in left tibia for past six months. Swelling appeared recently Slightly irregular swelling tender at lower end, of subcutaneous surface of upper third of tibia. No other bone lesions discovered. Wassermann negative

Early Paget's disease suggested as possible diagnosis by the late Sir Watson Cheyne Sixteen years later further investigations revealed typical changes in the skull tibiae femora and other bones. Had suffered little pain during the intervening years



FIG. 308

Case 96—Left tibia showing early Paget changes with typical pointed lower extremity the cortex, but with unusually uniform density Compare with Figure 306 Note early Paget changes in the fibula.

Fig. 302

Fig. 303

... gross increase in thickness—one and five-eighths inches at an ... but not of base. Fairly typical mottling. Figure 303 right arm showing ... in humerus and ulna and some atypical change in the radius.



Fig. 304

Case 94—Left side of pelvis and femur showing advanced changes of mixed honeycombed and striated types, and marked bowing of femur.

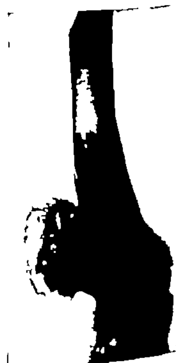


Fig. 305

Case 94—Knee joint showing typical changes in all three bones.

CASE 95—PAGET'S DISEASE

(Figs. 306 and 307) Male aged sixty five years. Had rickets in infancy. Fifteen years ago noticed hats were small after a year's wear. Head stopped growing two years ago. Has lost two and a half inches in height. General health good. Head large and lumpy on top. Right clavicle enlarged and right iliac crest thickened. Kypho-scoliosis rather marked with reduction of mobility. Considerable limitation of movement of hips except flexion. Slight general bowing of legs no obvious thickening. Skull pelvis and lower spine show typical changes. Left tibia shows very early disease below the tubercle. Pelvis is deformed. Diagnosed as Paget's disease five years ago.



Fig. 306



Fig. 307

[Ca]se 95—Figure 306 left tibia showing [v]ery early Paget changes in the region of the tubercle. Note the [ar]ea of decalcification with pointed lower extremity in the anterior cortex. Figure 307 pelvis and upper [fe]mora show Paget changes of various types including increased density. Note pelvis is deformed.

[C]ASE 96—PAGET'S DISEASE

[(F]ig. 308) Male aged forty two years. Complained of pain in [le]ft tibia for past six months. Swelling appeared recently. [Sl]ightly irregular swelling tender at lower end of subcutaneous [su]rface of upper third of tibia. No other bone lesions [di]scovered. Wassermann negative.

Early Paget's disease suggested as possible diagnosis by [the la]te Sir Watson Cheyne. Sixteen years later further [in]vestigations revealed typical changes in the skull tibiae [fe]mora and other bones. Had suffered little pain during the [in]tervening years.

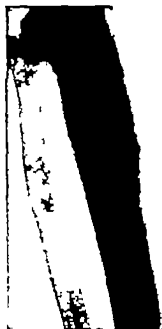


Fig. 308

Case 96—Left tibia showing early Paget changes with typical pointed lower extremity [in] the cortex, but with unusually uniform density. Compare with Figure 306. Note early Paget changes in the fibula.

CASE 97—PAGET'S DISEASE

(Fig 309) Male, aged seventy three years. Swelling of upper half of tibia for past few years. Typical Paget changes. Remainder of skeleton not investigated radiologically



Fig. 309

Case 97—Leg showing typical Paget changes in the tibia. Note the pointed lower extremity below and mottled increased density with some honeycombing above, and the calcified arteries. For comparison with the earlier lesions seen in Figures 306 and 308.

CASE 98—PAGET'S DISEASE

(Fig 310) Male aged forty-six years. Complains of headache and bronchitis for past eight months. Frontal headache especially on coughing and on certain movements of head and neck. No pain elsewhere. Slight deafness. No obvious thickening of skull. Nature of disease confirmed by biopsy of skull. Decompression operation had failed to relieve headache. Typical changes seen in films of skull, pelvis, sacrum, lower spine and upper ends of femora.



Fig 310

Case 98—Pelvis and upper femora, showing mixed changes of the striated and honeycombed types. Vertical striation in lumbar bodies present but not well seen.

CASE 99—PAGET'S DISEASE

(Fig 311) Female aged seventy years. Complained of pain at bottom of back and in knees for past five years. Worse after sitting. Marked kyphosis. Pigeon breast. Atheroma. Deafness. Bowing of femora and tibiae. Typical Paget changes in pelvis, both femora humeri radii and ulnae one tibia and fibula and the lower dorsal and lumbar vertebrae. One foot shows marked striation without new bone formation except a little on the calcaneum. In the arms increased density and thickening are the chief features a cyst is present in the upper third of one humerus.



FIG. 311
Case 99—Foot showing generalised striation of the bones. No hyperostosis present except on inferior surface of calcaneum.

CASE 100—PAGET'S DISEASE

(Figs. 312 to 314) Male aged fifty two years. Admitted for fracture of left humerus in lower third had sustained a fracture of the upper third of this bone eleven years previously at which time the bone was considered to be abnormal. Said to have fractured odontoid process of axis vertebra when thirty-one years of age this vertebra is now abnormal. Changes in bones of legs noticed for past four years. Wassermann negative Serum calcium 10·3 milligrammes and plasma phosphorus 3 8 milligrammes per 100 cubic centimetres. B.S R.—normal. Urine—normal. Typical changes found in skull both humeri, pelvis and both femora right tibia and upper third of left fibula. The fibular lesion is unusually cystic in appearance (Under Mr A. Compton and Dr F Parkes Weber)



FIG. 31
Case 100—Typical Paget changes in the lower end of the femur and in the tibia of the right leg, and atypical cystic enlargement of the upper third of the left fibula.





FIG. 313 FIG. 314

Case 100—Figure 313 left humerus showing a recent fracture. Note that the disease has invaded the mid-shaft and the lower extremity of the bone leaving the intermediate portion of the shaft almost unchanged. Figure 314 skull and upper cervical vertebrae showing changes in the axis vertebra as well as in the greater part of the calvaria.

CASE 101—PAGET'S DISEASE

(Fig 315) Female aged fifty-eight years. Fell while attempting to hang curtains. Admitted to hospital with fractured femur which was the seat of Paget changes.

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101 larg
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CASE 102—PAGET'S DISEASE

(Fig. 316.) Female aged forty-six years. Unusual case with facial bones involved. Operation for dental cyst thirteen years ago. Several subsequent operations on upper jaws. *Complains of aching in left maxilla at times.* Slightly deaf. Whole skeleton radiographed, but no bone affected other than the skull and superior maxillae. (By courtesy of Sir Frank Colyer.)



Fig. 316

Case 102—Skull showing typical Paget changes and also increased density of the maxillae. Note that the changes in the jaw are completely separate from those in the skull, a point against a diagnosis of leontiasis ossea.

CASE 103—PAGET'S DISEASE and OSTEOPOROSIS CIRCUMSCRIPTA

(Figs. 317 and 318.) Female aged sixty-six years. Complaining of increasing enlargement of upper part of skull on left side during past four months. Radiographs showed typical Paget changes in the skull, both ischia, right ilium, and several vertebral bodies. *Osteoporosis circumscripta* also seen in the skull. Wassermann negative. Serum calcium 10·4 milligrammes per 100 cubic centimetres. Two sisters of this patient also suffered from Paget's disease. (Under Dr H. Rast and Dr F. Parkes Weber.) (British Medical Journal 1937, 1, 318.)



Fig. 317

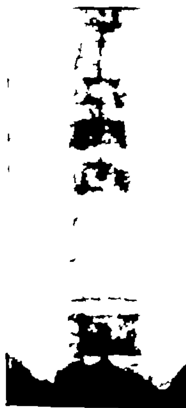


Fig. 318

Case 103—In Figure 317 the skull shows [illegible] irregular but considerable thickening with typical coarse texture and [illegible] sharply defined area of decalcification in the frontal region—osteoporosis circumscripta. In Figure 318 the spine shows increased density of certain vertebral bodies. Note irregular distribution of changes and fairly uniform density of the bones affected.



Fig 313



Fig. 314

Case 100—Figure 313 left humerus showing a recent fracture. Note that the disease has invaded the mid-shaft and the lower extremity of the bone leaving the intermediate portion of the shaft almost unchanged Figure 314 skull and upper cervical vertebrae showing changes in the axis vertebra as well as in the greater part of the calvaria.



CASE 101—PAGET'S DISEASE

(Fig 315) Female aged fifty-eight years. Fell while attempting to hang curtains. Admitted to hospital with fractured femur which was the seat of Paget changes.

Fig 315
Case 101—Left femur enlarged by Paget disease and with a typical transverse fracture at the usual site

CASE 102—PAGET'S DISEASE

(Fig 316) Female aged forty six years. Unusual case with facial bones involved. Operation for dental cyst thirteen years ago. Several subsequent operations on upper jaws. Complains of aching in left maxilla at times. Slightly deaf. Whole skeleton radiographed but no bone affected other than the skull and superior maxillae (By courtesy of Sir Frank Colyer)



Fig. 316

Case 102—Skull showing typical Paget changes and also increased density of the maxillae. Note that the changes in the jaw are completely separate from those in the skull, a point against a diagnosis of leontiasis ossea.

CASE 103—PAGET'S DISEASE and OSTEOPOROSIS CIRCUMSCRIPTA

(Figs. 317 and 318) Female aged sixty-six years. Complaining of increasing enlargement of upper part of skull on left side during past four months. Radiographs showed typical Paget changes in the skull, both ischia right ilium, and several vertebral bodies. Osteoporosis circumscripta also seen in the skull. Wassermann negative. Serum calcium 10·4 milligrammes per 100 cubic centimetres. Two sisters of this patient also suffered from Paget's disease. (Under Dr H. Rast and Dr F Parkes Weber) (British Medical Journal 1037 1 018)



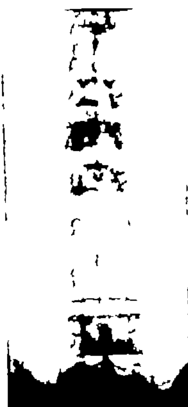


Fig 317 Fig. 318

Case 103—In Figure 317 the skull shows somewhat irregular but considerable thickening with typical coarse mottling and a sharply defined area of decalcification in the frontal region—osteoporosis circumscripta. In Figure 318, the spine shows increased density of certain vertebral bodies. Note irregular distribution of changes and fairly uniform density of the bodies affected



FIG. 313



FIG 314

Case 100—Figure 313 left humerus showing a recent fracture. Note that the disease has invaded the mid-shaft and the lower extremity of the bone leaving the intermediate portion of the shaft almost unchanged. Figure 314 skull and upper cervical vertebrae showing changes in the axis vertebra as well as in the greater part of the calvaria.



CASE 101—PAGET'S DISEASE

(Fig 315) Female aged fifty-eight years. Fell while attempting to hang curtains. Admitted to hospital with fractured femur which was the seat of Paget changes.

FIG 315
Case 101—Left femur enlarged by Paget's disease and with a typical transverse fracture at the usual site.

CASE 102—PAGET'S DISEASE

(Fig 316) Female aged forty-six years. Unusual case with facial bones involved Operation for dental cyst thirteen years ago Several subsequent operations on upper jaws. Complains of aching in left maxilla at times. Slightly deaf Whole skeleton radiographed but no bone affected other than the skull and superior maxillae (By courtesy of Sir Frank Colyer)



FIG. 316
Case 102—Skull showing typical Paget changes and also increased density of the maxillae Note that the changes in the jaw are completely separate from those in the skull, point against a diagnosis of leontiasis ossea.

CASE 103—PAGET'S DISEASE and OSTEOPOROSIS CIRCUMSCRIPTA

(Figs. 317 and 318) Female aged sixty-six years. Complaining of increasing enlargement of upper part of skull on left side during past four months. Radiographs showed typical Paget changes in the skull, both ischia right ilium, and several vertebral bodies. Osteoporosis circumscripta also seen in the skull Wassermann negative. Serum calcium 10·4 milligrammes per 100 cubic centimetres. Two sisters of this patient also suffered from Paget's disease (Under Dr H Rast and Dr F Parkes Weber) (British Medical Journal 1937 1 918)



FIG 317

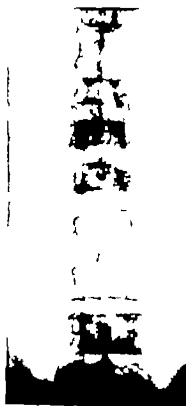


FIG. 318

Case 103—In Figure 317 the skull shows somewhat irregular but considerable thickening with typical coarse mottling and a sharply defined area of decalcification in the frontal region—osteoporosis circumscripta. In Figure 318, the spine shows increased density of certain vertebral bodies. Note irregular distribution of changes and fairly uniform density of the bodies affected.



Fig 313



Fig 314

Case 100—Figure 313 left humerus showing a recent fracture. Note that the disease has invaded the mid-shaft and the lower extremity of the bone leaving the intermediate portion of the shaft almost unchanged Figure 314 skull and upper cervical vertebræ showing changes in the axis vertebra as well as in the greater part of the calvaria.



CASE 101—PAGET'S DISEASE

(Fig 315.) Female aged fifty-eight years. Fell while attempting to hang curtains. Admitted to hospital with fractured femur which was the seat of Paget changes.

Fig 315

Case 101—Left femur enlarged by Paget's disease and with a typical transverse fracture at the usual site.

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(Fig. 316) Female aged forty six years. Unusual case with facial bones involved. Operation for dental cyst thirteen years ago. Several subsequent operations on upper jaws. Complains of aching in left maxilla at times. Slightly deaf. Whole skeleton radiographed but no bone affected other than the skull and superior maxillae. (By courtesy of Sir Frank Colyer.)



FIG. 316

Case 102—Skull showing typical Paget changes and also increased density of the maxillae. Note that the changes in the jaw are completely separate from those in the skull, a point against a diagnosis of leontiasis ossea.

CASE 103—PAGET'S DISEASE and OSTEOPOROSIS CIRCUMSCRIPTA

(Figs. 317 and 318.) Female aged sixty-six years. Complaining of increasing enlargement of upper part of skull on left side during past four months. Radiographs showed typical Paget changes in the skull, both ischia, right ilium and several vertebral bodies. *Osteoporosis circumscripta* also seen in the skull. Wassermann negative. Serum calcium 10·4 milligrammes per 100 cubic centimetres. Two sisters of this patient also suffered from Paget's disease. (Under Dr H. Rast and Dr F. Parkes Weber.) (British Medical Journal 1937, 1, 918.)



FIG. 317

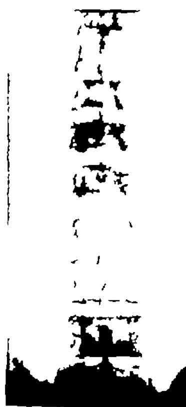


FIG. 318

Case 103—In Figure 317 the skull shows somewhat irregular but considerable thickening with typical coarse mottling and a sharply defined area of decalcification in the frontal region—osteoporosis circumscripta. In Figure 318, the spine shows increased density of certain vertebral bodies. Note irregular distribution of changes and fairly uniform density of the bodies affected.

CASE 104—PAGET'S DISEASE complicated by SARCOMA

(Figs. 319 to 321.) Female aged seventy-six years. Gradual onset of pain in left groin during past four months not affected by rest or exercise. Pain much aggravated by a recent fall. *All movements of left hip limited by severe pain. Indefinite swelling in left groin* skin temperature raised veins prominent femoral artery pushed forwards by the swelling. Alkaline phosphatase in blood raised. No evidence of Paget's disease in any bone except the pelvis. Radiograph of chest shows left ventricular enlargement but no sign of metastases. Treated with Coley's fluid and X ray therapy without benefit. Swelling increased. Numerous metastases appeared in the lungs with left pleural effusion, and she died four months after first examination. Microscopic section confirmed the diagnosis of Paget's disease and showed the growth to be a chondrosarcoma. (Under Mr S. A. Jenkins.)



FIG. 319

Case 104—Pelvis and hips showing irregular increased density of left side of pelvis with signs of sarcomatous growth in the ilium.



FIG. 320



FIG. 321

Case 104—Figure 320 a microscopic section of fragment from the pelvis, shows the typical mosaic structure of the bone, and the marrow spaces filled with loose myxomatous fibrous tissue (×50). Figure 321 is a microscopic section from the tumour area showing the chondrosarcomatous nature of the pelvic growth (×80)

CHAPTER 24

INFANTILE SCURVY

Barlow's Disease

This condition is a deficiency disease due to inadequate absorption of vitamin C, the chief feature being a tendency to haemorrhage. According to Still (193) the difference between infantile scurvy and rickets, which at one time were so often combined and constantly confused, was pointed out by Glisson as early as 1650, but this was forgotten for more than 200 years till Cheadle in 1878 again called attention to the distinction between the two diseases. Barlow's first paper appeared in 1883. It is to these two men, Cheadle and Barlow, that the world owes a clear understanding of the scorbutic nature of this condition and its ready response to treatment with fresh food such as fruit juice and raw meat juice. Valuable modern accounts of the disease have been contributed by Sheldon (1940) and Graham (1947), and an admirable description of the radiological features by Hunter and Jupe (1939).

Hereditary and familial influences play no part in the incidence of scurvy, at any rate in Europe. Breast-fed infants never develop the disease in this country, but this is not entirely true of the Far East, since in that part of the world the mother's milk may be so lacking in vitamin C that the suckling child develops scurvy.

Age.—It is a disease of the second half year of life, occurring usually from the sixth to the fifteenth month, and is rarely seen before or after this period. We know of only two cases of scurvy in older patients that have been reported in this country in recent years (Cassidy 1922 and Pugh 1925); these were both males, aged eighteen and eleven years respectively.

Sex.—Both sexes are affected to an approximately equal extent.

Etiology.—The cause is lack of the water-soluble vitamin C, resulting from the absence from the diet of fresh milk, both the mother's and cow's milk, and failure to make good the deficiency by giving the juice of fresh fruit and vegetables or uncooked meat juice. The cause of the haemorrhagic diathesis is still obscure; all that is known with certainty is that it is not due to lack of vitamin P, which is concerned with capillary fragility. The two lads reported respectively by Cassidy and Pugh had both displayed a long continued aversion to the consumption of fruit and vegetables.

Signs and symptoms.—There may be indefinite prodromal symptoms such as failure to thrive, anorexia, irritability, increasing pallor and anaemia, but the distinctive signs usually have a sudden onset. Often there is fever, which may or may not be accounted for by some definite minor ailment, most commonly one affecting the respiratory tract—in 12 per cent. according to Dogramaci (1946)—which is regarded as precipitating the activity of an unsuspected latent scurvy. The most frequent distinctive signs result from subperiosteal haemorrhages, which produce visible and palpable swelling of one or more limbs, accompanied by pain and tenderness. The infant abruptly loses the use of the affected limb—the so-called pseudo-paralysis, though no actual paralysis is discoverable. The limb may be oedematous. The most striking feature is often the excessive tenderness of the limb; even the gentlest handling may produce a piercing shriek of agony, a very different cry from that resulting from mere discomfort or fretfulness. The subperiosteal haemorrhages begin close to the epiphyseal lines and spread along the shafts. The common sites for swelling are the lower ends of the femur and humerus, the tibia and fibula, the distal extremity of the radius, and the costo-chondral junctions. The joints are unaffected but epiphyses may become separated. The sternum and costal cartilages are sunk backwards from the level of the ribs and there

is some beading but the costo-chondral junctions are not particularly tender the picture differs considerably from the typical chest of rickets. In a proportion of the cases the abrupt backward displacement of the costal cartilage in relation to its rib warrants the name of bayonet deformity There is considerable difference of opinion as to the frequency of this. Haemorrhage on the skull has been described, and the palate or the orbit may be affected the latter being revealed by proptosis with or without a black eye. Bleeding from spongy gums is a well-known and common feature. The gums around the teeth are swollen, purple in colour and bleed readily Occasionally the teeth fall out. It is said that spongy gums occur only if some teeth have erupted, but this is not entirely true. The gums over teeth that are about to erupt usually the central incisors may be found swollen and purple. Haemorrhage from the kidneys is not uncommon, and may be a diagnostic sign of considerable value but it is readily overlooked unless specially looked for by microscopical examination of the urinary sediment obvious haematuria is quite exceptional. Other occasional sites of bleeding are the skin in the form of ecchymoses and petechiae the nose lungs, brain and viscera blood may be found in the stools, unassociated with any pain The teeth are imperfectly formed. The case of scorbutic infantilism reported by Cassidy (1922) had severe pyorrhoea from the age of thirteen years and later developed haemorrhagic swellings of the muscles of the calves and the hamstrings. He had severe pain and tenderness of the legs the lower ends of the femora were exquisitely tender In spite of every effort to prevent them, contractures developed.

Blood Examination—The anaemia, which is the direct result of lack of vitamin C rather than of haemorrhages is of the orthochromic and normocytic types (Parsons and Smallwood 1935) Bleeding and clotting times are normal. The alkaline phosphatase is always below normal (Smith and Maizels 1932 Dogramaci 1946) The ascorbic acid in the plasma drops to nil (McIntosh 1949) but a single estimation of the amount in the plasma or urine is said to be of no value more elaborate investigations being necessary (Graham 1947)

Radiographic appearances—There is a loss of density and pattern of the cancellous bone to be seen in the epiphyses as well as in the metaphyses and shafts of the long bones. The cortex is thinned and forms a conspicuous fine line limiting a ground glass area formed by cancellous bone According to Park *et al* (1935) an early sign at the wrist is fuzziness at the outer corner of the radius. Later this becomes a crevice and spreads across the metaphysis to form a clear zone which indicates a partial arrest of osteoblastic activity (Hunter and Jupe 1939) The depth of this zone varies with the severity of the disease similar changes occur in the ulna and at the more rapidly growing ends of other long bones At the extremity of the metaphysis between the clear zone and the epiphysis is a dense line formed by the lattice referred to later this is the "white line of Fraenkel (1908) This dense line projects at its extremities to form a spur sometimes referred to as the lateral spur of Pelkan (1925) The line becomes thicker as the disease increases in severity Together with the epiphysis it appears to be loosely attached to the end of the shaft a certain amount of actual displacement is not uncommon. In exceptional cases the displacement of an epiphysis may be complete in two cases published by Scott (1941) and Hudson *et al* (1941) respectively the head of the humerus was completely displaced in both shoulders. Bilateral displacement of the lower femoral epiphysis was reported by Neale (1949) Owing to arrest of growth the epiphyses and the carpal and tarsal bones may show a ring of increased density surrounding a translucent centre—Wimberger's sign (1925)—but this should not be regarded as diagnostic of scurvy This feature is well seen in the astragalus and os calcis in some cases. When the disease has been arrested the dense ring becomes surrounded by bone of normal density (McIntosh 1949) The central translucent areas in the epiphyses may be visible for as long as five years after arrest of the disease (Hunter and Jupe 1939) A subperiosteal haemorrhage which constitutes such an important clinical feature is not visible in a radiograph until

ossification commences in the haematoma and this does not occur till about ten days have elapsed since the commencement of treatment (Park *et al* 1935). At first only a thin curved line indicates the limit of the haematoma which surrounds the bone for a varying distance along the shaft. Later the whole area of the haemorrhage becomes dense but if efficient treatment is now adopted complete absorption of the haematoma will occur in two or three months if not sooner. The anterior ends of the ribs are expanded to a marked degree but do not show "cupping."

The two older cases already referred to were singularly alike. The chief feature besides rarefaction of the bones was the presence of dense structureless opacities at the ends of the shafts of the major long bones with a tendency in the lower femur and upper tibia for these opacities to be conical in shape particularly in Cassidy's case.

Progress—Though at one time a limited number of the cases ended fatally this never occurs nowadays. All the skeletal changes eventually disappear.

Complications—Complete separation of an epiphysis already referred to only occurs exceptionally. Pyelitis and diarrhoea have been seen in some cases.

Pathology—The dense line next to the growth disc consists of calcified cartilaginous matrix the so-called "lattice" a feature seen also in congenital syphilis (Park *et al* 1935). In this layer the provisional calcification is excessive because its normal destruction and replacement by bone are largely arrested owing to want of osteoblastic activity (Fig 328A). Microscopic fractures may be seen in the lattice. In the clear zone next to the lattice rarefaction has taken place the trabeculae being thin and widely separated. An abundance of osteoblasts may be seen but they are incapable of forming bone matrix because of the lack of vitamin C. There is no osteoid to be seen. The marrow cells have disappeared and the marrow spaces are filled with "loose embryonic like connective tissue" (Fig 328B). These changes in the clear zones are best seen at the more rapidly growing ends of the long bones. Reduction in the density of the bones is general but is most marked in the metaphyses. The periosteum is said to be loosened (McLean and McIntosh 1928). Subperiosteal haemorrhages originate in fractures of the lattice and the adjacent thinned cortex.

Diagnosis—The radiographic appearances of the metaphyses in scurvy are very similar to those of congenital syphilis in which a dense "lattice" is also formed. An important point of distinction is the age of the patient. Congenital syphilis reveals itself in the first six months of life while scurvy occurs in the second six months. The clear band is deeper and the dense line more uneven in syphilis while the periosteal shadows are different and the lesions more symmetrical. In the absence of other non-skeletal signs of syphilis the Wassermann and Kahn tests should settle any doubts, though a single negative Wassermann is not absolutely conclusive. Difficulties should not arise in distinguishing scurvy from cretinism and from poisoning by phosphorus lead or bismuth in which the density at the end of the shaft is a band of some width, not a "dense line" which is all it usually amounts to in scurvy. Scurvy has been mistaken for osteomyelitis on many occasions. If the presence of leucocytosis and the degree of fever are insufficient to eliminate doubts anti-scorbutic treatment should produce dramatic improvement in two or three days if the case is one of scurvy. The pseudo-paralysis may suggest a diagnosis of poliomyelitis but the extreme pain and tenderness the site of the latter near the ends of the shafts and the prompt response to treatment should settle the matter in favour of scurvy. Lastly the radiographic appearances may be simulated by leukaemia, but otherwise the two diseases have nothing in common.

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CASE 105—INFANTILE SCURVY

(Figs. 322 and 323) F. S. male aged nine months. Has been fed on patent foods. Twelve days ago had a fall. Left knee tender and cannot be fully extended. Slight indefinite swelling of lower third of left femur which is very tender. Gums are spongy adjacent to the left lower incisor tooth and over the crowns of the prominent but unerupted upper incisors.

Fig. 322

Case 105—Knees showing the formation of a clear crevice just below the inner part of the dense "lattice" at the lower end of both femoral shafts. The tibiae and fibulae show only the early formation of the dense line.



Fig. 323

Case 105—Lateral view of left knee showing in the femur the dense "lattice" and an early stage in the development of the clear crevice anteriorly.

CASE 106—INFANTILE SCURVY

(Figs. 324 and 325.) T. M., male, aged ten months. Two months ago caught foot against his other foot and screamed with pain. Later cried a lot at night and seemed ill. Something clicked in his back and he would not put knees down. Was able to sit up but cannot do so now. Has been fed on patent foods throughout, but was given some fresh milk at time the symptoms commenced. Seemed to lose use of one leg and now the other. Poliomyelitis suspected. Screams when hands are touched. Pale child. Head large, fontanelle open. Spongy gums around teeth in both jaws. Left thigh and leg swollen, lower end of femur and whole tibia thickened. Lower end of right femur also thickened. Wrists swollen, with thickening of lower ends of radius and ulna. Spine, rickety kyphosis.



Fig. 324



Fig. 325

Case 106. Fig. 324.—Forearm showing rarefaction of bones, with dense line at extremities of radius and ulna. On the ulna the dense line forms a spur, the "lattice" and epiphysis being displaced inwards from the line of the shaft. There is only faint evidence of clear bands adjacent to the dense lines. Fig. 325.—Leg and foot showing poorly calcified bones, dense lines at the extremities of the tibial and fibular shafts, and shadows indicating commencing ossification in the subperiosteal haematomata extending up the shafts.

CASE 107—INFANTILE SCURVY

(Fig. 326.) J. B., male, aged ten months. Born at eighth month by Caesarean section. Fed on patent food, but with some fruit juice. Some clinical signs of rickets in addition to those of scurvy affecting both arms and legs. Has haematuria. (Under Sir R. Hutchison.)



Fig. 326

Case 107.—Legs showing well marked dense lines forming spurs on either side of the ends of the shafts. A clear band adjacent to the dense line is visible in some places. Evidence of ossification in subperiosteal haematomata is to be seen on both femora and both tibiae. The epiphyses at the knees are noticeably clear and translucent, but are outlined by denser bone.

CASE 108—INFANTILE SCURVY

(Fig 327) M B girl, aged nine months. Bottle fed. Colour good. Left leg tender for past week with some swelling Left leg is swollen particularly the lower third, and skin feels warm but is not red. No fluctuation to be felt. Radiographs showed an ossified haematoma surrounding the lower half of the left femur This suggested the disease had been present for a considerable time certainly longer than a week and that healing was taking place.



Fig. 327

Case 108—Left leg showing typical app ar nc of subperiost al haematoma of the femoral shaft in which ossification is well advanced.

CASE 109—INFANTILE SCURVY

(Fig 328) (After Park *et al.* by kind permission of Archives of Diseases in Childhood.)

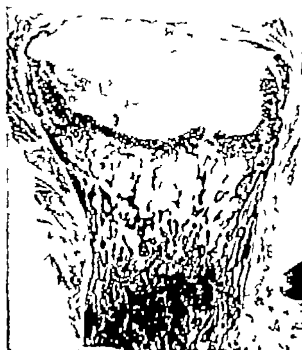


Fig 328A

End of rib showing the lattice of calcified cartilage fractured in places, and, below this, deficient bone formation at the extremity of the metaphysis



Fig 328B

Bone from the clear zone showing characteristic scorbutic changes The marrow cavity is filled with loose embryonic-like connective tissue ery few marrow cells p esent Haem rrh g ha occurred in part of the field

CASE 110—SCURVY IN LATE CHILDHOOD

(Figs. 229 and 230.) Boy aged twelve years. Healthy till five years when he had severe attack of influenza and rheumatism. At seven years bones began to bend; had sharp pains in legs and for over three years was confined to his room. Has always shown a strong objection to vegetables and fruit. Decidedly dwarfed. Height 47 inches (normal 63½ inches). Deformities confined to lower limbs. *Bow-leg on right and genu valgum on left with marked curvature of left tibia and fibula.* The epiphyses of the leg bones are enlarged while the shafts are very slender. Movements of the hips, knees and ankles are restricted. The pelvis, spine, chest and upper limbs are fairly normal but the arms and wrists are slender. Calcium content of blood and urine normal. Radiographs showed general hypocalcification of the skeleton particularly marked in the pelvis, vertebrae, hands and feet, scapulae and upper ends of humeri. No sign of rickets at the wrists. In the lower limbs at the ends of the shafts of the long bones, are *concentrations of lime salts producing more or less triangular shadows.* Antiscorbutic treatment with an abundance of all vitamins resulted in a gain in weight but little change had occurred in the bones after eighteen months. A fall from his wheel-chair resulted in fracture of the left tibia. (Under Dr W. T. Gordon Pugh.)



Fig. 229

Case 110—Femora showing, in spite of treatment, general hypocalcification with striking degree of increased density at the lower ends of the femora and upper ends of the tibiae and fibulae mostly but not entirely in the metaphyses.



FIG. 530

Case 110—Legs showing the abnormally translucent bones, curvature of the left tibia and fibula, fracture of the left tibia and irregular areas of greatly increased density in the lower ends of the bones of both legs

RICKETS

Rickets is a deficiency disease affecting the growing child or adolescent. It is a metabolic disorder resulting in defective calcification of growing bone. It is characterised by readily recognised changes at the epiphyseal lines in addition to a general lack of density of the bones. Cases may be grouped according to the age of the patient and the response to treatment as follows: Foetal, Infantile, Resistant or Continued and late or Adolescent Rickets. For those resistant cases in which the onset is late, McCance (194[illegible]) has suggested the name of Acquired R.R.D. (Raised Resistance to Vitamin D). Osteomalacia is now universally regarded as rickets occurring in adults, i.e. after skeletal growth has ceased. The bone changes in Coeliac Disease are essentially rachitic, while those in Idiopathic Steatorrhoea are osteomalacic.

FOETAL RICKETS

True foetal rickets is a very uncommon condition but it certainly does occur provided the mother is suffering from sufficiently severe osteomalacia or, in some cases, late rickets as a result of deficiencies in both diet and light, a state of affairs frequently met with in the East, but not in this country. More commonly hypocalcification without special signs of rickets is seen affecting the foetal skeleton in such cases. In 1934 Maxwell reported sixteen cases seen in China with convincing radiographic evidence of the presence of foetal rickets. Practically all the mothers of these cases were suffering from definite osteomalacia. Examination of blood taken from the umbilical cord in a number of the cases showed the serum calcium varied from [illegible]·6 mg. to 10·8 mg. per 100 c.c.—in only two was the figure below 8 mg.—and the plasma phosphorus in four cases varied from 2·6 mg. to 4·4 mg. per 100 c.c., while in a fifth it was as high as 8·8 mg. It was noted that the teeth showed imperfect formation when erupted later. Snapper (1949) also published two cases of definite foetal rickets. Mellanby (1934) reported that he and his wife had succeeded in producing foetal osteoporosis in animals but had never been able to produce foetal rickets.

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CASE 111—FOETAL RICKETS

(Fig. 331.) Child born by Caesarean section. On the third day developed attack of melaena neonatorum. In spite of transfusion child died sixty-five hours after birth. Marked rachitic rosary and Harrison's sulcus present. Serum-calcium in cord blood was 10·0 mg. per 100 c.c. The mother was suffering from osteomalacia, with pelvic deformity which had developed as a result of starvation, a little over two years before this child, her sixth, was born. Radiographs showed typical rachitic changes in the infant. (Published by Professor J. P. Maxwell, Journal of Pathology and Bacteriology, 1932, 3[illegible], 419.)



FIG. 331.
Case 111.—Forearm on day of birth, showing definite signs of rickets commencing in foetal life. (By courtesy of Professor Maxwell and the Journal of Pathology and Bacteriology.)

CHAPTER 26

INFANTILE RICKETS

Though much less common than it was owing to improved economic conditions and the better instruction of mothers this is still the most common type of rickets. As in all types of rickets skeletal growth is essential for its occurrence It is characterised by bossing of the skull enlargement of epiphyses bending of the long bones and retarded growth.

Hereditary and familial influences are usually more apparent than real the exceptional incidence of the disease in some families depending on the same errors of diet and mode of life being committed during the infancy of each individual member In India, however the child of an osteomalacic mother—if not born with foetal rickets—is prone to develop the disease later this is particularly true if the osteomalacia of the mother is severe (Green Armytage 1928 1934)

Sex—The sexes are equally liable to the disease

Age—It may develop at any time during the first few years of life but the most common age for the onset is from nine to twelve months. It may occur as early as the third month, and may continue to increase in severity up to eighteen months or more.

Etiology—The essential cause is lack of vitamin D owing to inadequate or unsuitable diet and deficient exposure to sunlight The lack of vitamin D upsets the calcium and phosphorus metabolism and leads to imperfect calcification of the growing skeleton Improper though plentiful food may account for its occurrence the fault being a lack of ergosterol, from which vitamin D is synthetised in the skin by sunlight. A high carbohydrate diet favours the onset of rickets. It is more common in late winter and early spring, and during a war which causes a serious reduction in the food supply of a nation A premature child in whom neonatal growth may be rapid is prone to the disease. In North China rickets and tetany are not infrequent in the first few months of life because the milk of the osteomalacic mother is deficient in vitamin D while foetal and late rickets and osteomalacia are all relatively common on the other hand, infantile rickets is not often seen in that country at the usual age for this affection (Snapper 1940) As already indicated at least potential growth is essential for the development of rickets.

Distribution—The whole skeleton is affected, at least to some extent.

Signs—The general appearance of a case of moderate severity is typical and diagnostic at sight. The large head with prominent forehead the retarded growth even amounting to dwarfism the deformed chest and prominent abdomen the enlarged epiphyses and excessive curvature of some of the long bones together constitute a characteristic picture. The dwarfism when present, is of the short-limbed type. In the younger infants, those under six months, thinning of the skull in the occipital and parietal regions—cranio-tabes—may be present, and is recognised by the characteristic egg-shell crackling on palpation Later the frontal and parietal eminences display obvious bossing—Parrot's nodes—while the anterior fontanelle remains large and its closure is delayed Viewed from above the shape of the vertex may warrant the term hot-cross-bun head. Sweating of the head may be a noticeable feature The younger the child the more likely is the skull to be affected and the older the child the more often do the lower limbs show most deformity (Parsons 1934) The child is often restless and irritable. The chest deformities include the well-known rickety rosary and transverse Harrison's sulcus. There may be some pigeon breast though this is not necessarily rachitic in origin. If the child is kept on his back for long the chest will flatten from before backwards. The condition of the spine depends on whether or not walking has begun If the child can sit but not walk, the spine assumes a long kyphotic curve, increasingly accentuated from above down the greatest convexity being in the upper lumbar region. If the child has been able to get about on his feet for an appreciable time the deformity in the lower portion

of the spine is reversed when he is standing the kyphosis being replaced by lumbar lordosis with prominence of the buttocks and abdomen Scoliosis may complicate the deformity In the limbs there is enlargement of the ends of the bones and accentuation of the normal curves of the shafts The enlargement of the lower epiphyses of the radius and ulna is a readily assessed deformity while the wrists are particularly suitable for radiological examination to determine the presence and activity of rachitic changes at the epiphysial lines Bow legs and genu valgum are common deformities in severe cases curvature of the forearms and of the humeri may be seen When the child cannot walk and spends much time sitting with his legs crossed and his knees turned out outward bowing of the tibiae particularly in the lower thirds develops. When walking becomes increasingly possible weight-bearing may produce spontaneous correction of these curves provided they are not too severe and the bones not too soft The amount of spring in a curved tibia on attempting to bend it is a useful guide as to the plasticity of the bone and the necessity for splintage When walking has not been delayed or the onset of the disease has been later than usual genu valgum often with some degree of outward bowing of the tibiae below is the usual deformity If the femoral shafts have yielded to weight bearing the deformity consists of an antero-external bend with or without a reduction in the angle of the neck of the bone. A horizontal position of the femoral neck, with limitation of abduction of the hip joint may be due entirely to bowing of the femoral shaft though it is frequently mistaken for true coxa vara. The muscles are flabby and the ligaments lax so cases are often late in standing and walking and their gait is waddling In severe cases movements may be painful Owing to the thoracic deformity the liver and spleen may lie below their normal positions. Dentition is delayed and the enamel and dentine may be imperfect (Mellanby 1934)

Blood examination—Though not part of the disease anaemia may be present The serum calcium is normal in amount but may be rather low the plasma phosphorus is low the alkaline phosphatase is raised the amount varying with the activity of the disease so the quantity may be of some value in determining the response to treatment

Radiological appearances—Radiological signs precede the clinical signs and are to be found particularly at the more actively growing epiphysial lines at the knees wrists and costochondral junctions. By far the most convenient guide is an antero-posterior radiograph of a wrist both for determining the diagnosis and for assessing the effect of treatment The depth of the epiphysial lines is increased particularly in severe cases. The metaphyses are enlarged and the ends of the shafts are irregular with loss of definition and cupping There is also general hypocalcification of the bones and the cortices are reduced in density A layer of less dense bone may be seen on the surface of the cortex particularly when healing has commenced (Wimberger 1925) In the hips true coxa vara may be present the angles of the femoral necks being reduced with widening and irregularity of the epiphysial lines. The pelvis may be funnel-shaped or triradiate occasionally it is flattened antero-posteriorly The degree of curvature of the shafts of the long bones can be accurately assessed the curve in a shaft is buttressed by additional bone on the concave side The spine is diminished in density and the vertebral bodies show a tendency to be biconcave while the discs are biconvex The skull is thickened on its outer surface where bossing has occurred. On the inner side of the tibia, in its upper third may be seen a projection from the cortex not unlike an exostosis but only in a few cases. This feature is usually but not invariably bilateral and absolutely symmetrical no other "exostoses" are found elsewhere in the skeleton.

Progress—If untreated the hypocalcification and deformities become progressively more marked. If treated efficiently improvement sets in rapidly and the irregular proliferation at the epiphysial lines gives place to normal growth calcification and ossification proceed normally and excess of osteoid is no longer seen If a radiograph of a wrist is now taken commencing healing is revealed by transverse linear shadows close to and parallel to the surfaces of the epiphyses this indication of the resumption of normal calcification and

INFANTILE RICKETS

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CASE 112—INFANTILE RICKETS

(Figs. 332 and 333.) C. S., female. Attended hospital when nine weeks old for swelling of limbs. Radiographs revealed periostitis and metaphysial changes due to congenital syphilis. This was successfully treated, but when sixteen months old the child attended with typical rickets, which was still active when radiographed at two years. Child died of broncho-pneumonia following whooping-cough shortly afterwards. (Under Dr Donald Paterson.)



FIG. 332

Case 112.—Elbow and wrist at two years, showing defective calcification of the bones, a healed fracture of the radius and typical cupping of the radial and ulnar metaphyses.



FIG. 333

Case 112.—Section of an epiphysial line from this case. Note the absence of cartilage cell columns and of calcified cartilage zone, and the irregular masses of cartilage and some osteoid, where there should be normally ossified cancellous bone.

ossification is located where these would have occurred had there been no rickets *i.e.* near the epiphyses and not close to the ends of the shafts this is the so-called line test The metaphysis becomes stippled and the cupping and other changes gradually disappear The density of the skeleton as a whole is improved, but there may be coarse trabeculation for some time The bones tend to straighten if the deformities are not too severe.

If growth ceases for any reason—not necessarily on account of age—the progress of the rachitic changes ceases for a time irrespective of whether or not the case is being treated.

Complications—Only a small proportion of cases have tetany the spasmophilic manifestations take the form of laryngismus stridulus, carpo-pedal spasms, and convulsions Rickety children are prone to bronchitis. Fractures are not uncommon and are often of the greenstick variety In the very severe cases with marked generalised hypocalcification of the skeleton, multiple spontaneous fractures may occur and doubts may arise as to whether rickets is entirely responsible or whether it has been superimposed on osteogenesis imperfecta, as was suggested in a case reported by Langmead (1920) In a case of this sort reported by Bevan (1937) a child of two years several of the fractures were so wide and devoid of callus that they were distinctly suggestive of Looser s zones as seen in cases of Milkman s syndrome in adults. We have seen an infant in whom most of the metacarpals were fractured. In another case we saw the skeletal signs of congenital syphilis which was treated successfully give place to those of rickets in the course of a few months.

Pathology—At the epiphyseal lines there is a failure of the normal formation of cartilage columns and this is replaced by excessive and irregular proliferation of the cartilage cells. Instead of normal calcification of the cartilage and its transformation into bone there is an abundant production of osteoid tissue and inadequate formation of bone. As Parsons (1934) says there is a substitution of disorder for order Compared with renal rickets the amount of fibrous tissue formed in the adjacent marrow is negligible In the medulla there is an increase in the amount of fat Under the periosteum of the long bones there is a rounding off of angles, and buttressing of the increased curves The bones are soft and can be cut with abnormal ease. In the skull an abundance of partially calcified subperiosteal osteoid accounts for the bossing The enlargement at the costo-chondral junctions responsible for the rickety rosary is much more obvious on the inner than the outer aspect of the chest wall Secondary hyperplasia of the parathyroids has been reported (Minor and Pappenheimer 1921) this is probably an uncommon occurrence and of no clinical importance

Diagnosis—In infants the diagnosis presents little if any difficulty when the activity of the disease is in doubt a radiographic film of one wrist should settle the matter It is when the rickets is prolonged or develops late that the presence or absence of coeliac disease or of renal osteo-dystrophy has to be settled by appropriate investigations In a particularly severe case with fractures there may be difficulty in excluding osteogenesis imperfecta as at least in part responsible for the condition of the skeleton.

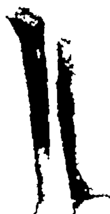
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CASE 112—INFANTILE RICKETS

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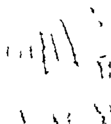


Fig. 332

Case 112.—Elbow and wrist at two years, showing defective calcification of the bones, a healed fracture of the radius and typical "cupping" of the radial and ulnar metaphyses.



Fig. 333

Case 112.—Section of an epiphysial line from this case. Note the absence of cartilage cell columns and of a calcified cartilage zone, and the irregular masses of cartilage and some osteoid where there should be normally ossified cancellous bone.

CASE 113—INFANTILE RICKETS

(Figs. 334 and 335.) E. D. male aged four years. Had fits when an infant; none since two years. Walked at sixteen months. Ankles became deformed about two months later with some limping. Never treated for rickets. On examination: coxa vara, curved tibiae, beading of ribs, enlarged epiphyses especially at wrists. Urine normal.



FIG. 334

Case 113—Wrist and hand showing rachitic changes, "cupping" of the radius and ulna and poor calcification of all the bones.

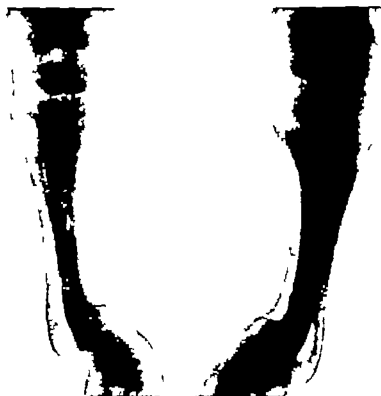


FIG. 335

Case 113—Legs showing rachitic changes at the epiphyseal lines of the femora and tibiae and deformity of the tibial and fibular shafts.

CASE 114—INFANTILE RICKETS

(Fig 336) V R. female aged two years and five months. Has been treated for rickets which is now practically healed Deformities still present Exostoses present on inner side near upper end of shafts of both tibiae



Fig. 336

Case 114—Legs showing disease practically healed, but deformities still present. Note the exostoses projecting from the upper part of both tibiae

CASE 115—INFANTILE RICKETS (severe)

(Fig 337 and 338) D C., female aged four years and nine months. Did not walk till two and a half years old. Six months ago had pneumonia has not walked since. No history of fractures. Pale fretful child. Under-sized. Unable to stand without help Head large with forehead bulging Sclerotics not blue. Teeth not translucent. Rickety rosary Abdomen protuberant. Bowing of forearms. Femoral curvatures exaggerated. Tibiae bowed anteriorly in lower thirds. All epiphyses enlarged. Examination of urine and faeces revealed nothing abnormal. Radiographic examination showed advanced rickety changes and several healed fractures. (Under the late Sir Henry Gauvain.)



Fig. 337

Case 115—Antero-posterior and lateral views of right forearm showing general hypocalcification of the bones widening of the epiphysial lines, with "cupping" of the radial and ulnar shafts at the wrists, and old fractures.



Fig. 338

Case 115—Legs showing advanced rickety changes Note the layer of particularly poorly calcified bone beneath the periosteum of the shafts in some places

CHAPTER 27

RESISTANT OR CONTINUED RICKETS

The majority of cases of rickets respond more or less readily to suitable treatment but a limited number continue to show typical changes in the skeleton in spite of vigorous treatment with vitamin D and only begin to heal when the number of units of vitamin D given daily is increased considerably sometimes to spectacular amounts Albright *et al* (1937) write of "intrinsic resistance" to vitamin D in such cases they report a case which though it had resisted treatment for ten years was eventually cured by colossal doses of vitamin D given by mouth. McCance (1947) describes the exceptional resistance in such cases as "congenital" in contrast to those in whom the raised resistance is "acquired" later In some cases relapses occur if the daily dosage of vitamin D is not maintained at a comparatively high level (Bakwin *et al* 1940) occasionally it is found that the amount required to prevent relapse fluctuates (Mackay and May 1945) Occasionally the disease may be aptly described as intermittent or relapsing Continued rickets as well as late rickets is much commoner in India and the Far East than in this country but this appears to be due more to lack of adequate treatment than to exceptional resistance to vitamin D In Britain "resistant rickets" is the more correct term for these cases which are definitely uncommon though it is more often met with than "late rickets." Included under this heading are the cases of infantile rickets who in spite of ordinary treatment still show signs of active rickets when they have reached the age of four or five years or are even considerably older Unusual resistance to treatment may however be realised before this age is reached (Gill 1930)

Hereditary and familial influences—Familial influence is sometimes met with (McCance 194) and occasionally heredity appears to be playing a part

Sex—Study of some thirty cases including a dozen personal cases indicates that girls are twice as prone as boys to exhibit an exceptional resistance to vitamin D (G>B)

Age—The ages in this series varied from five to eighteen years nine cases were ten years of age or older

Signs and symptoms—The sufferers feel weak and are readily fatigued exceptionally walking is impossible If not actually dwarfed they are shorter than normal the degree of reduction in stature no doubt depending on the date of onset and the duration of the disease They exhibit the usual enlarged epiphyses and deformities of rickets.

Blood examination—The plasma phosphorus is usually low and the serum calcium is normal or slightly reduced in amount As in all types of rickets the alkaline phosphatase is *high* Only exceptionally is the plasma phosphorus not low in two brothers aged thirteen and nine years reported by Gill (1930) the plasma phosphorus figures were unusual, being 4·0 and 5·7 milligrams per 100 cubic centimetres respectively

Radiographic appearances—Typical rachitic changes are seen at the epiphysial lines. The general hypocalcification may be severe and multiple fractures may be present (Albright *et al* 1937 Mackay and May 1945) On the other hand the porosity of the bones may be accentuated locally so that cyst-like islands of decalcification are seen clear areas of this type were present in a femur and a radius respectively in two cases reported by Mackay and May and in a femur and tibia of a girl of ten years in the care of the present author this girl's sister also suffered from continued rickets. Digital markings are seen in the skull in some cases. Symmetrical projections, like exostoses, from the upper part of the tibia on the inner side are rather more frequently seen than in cases of ordinary rickets

When growth ceases the rachitic changes cease even though the cause is still operative and the bones remain porotic. The hips seem to be the first and the wrists the last to show healing of the epiphysial line changes presumably this depends on the earlier cessation of growth at the upper ends of the femora.

Diagnosis—Owing to lack of an adequate history difficulty may be experienced in deciding whether a case should be regarded as suffering from continued or late rickets this difficulty is also experienced with some of the published cases. In every case it is advisable to exclude coeliac and renal disease by appropriate examination of the faeces and the urine.

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M CRAY H nd MAY Q (1945) Proceedings of the Royal Society of Medicine (Section for the Study of Disease in Children, 23) 38, 563.

CASE 116—RESISTANT RICKETS

(Figs. 339 to 341.) J. S. female aged five years and ten months when first seen in 1940. Very carefully fed but not on breast. She walked at fifteen months but three months later legs were noticed to be bowed. Splintage applied. Has always had a rolling gait. Legs still bowed but not getting worse. Tires readily. Getting fatter lately. One brother normal. Healthy looking child below normal in height. Arms rather short. Head not enlarged. Rather fat and heavy. Marked lordosis. Abdomen very large, liver and spleen not enlarged. Some enlargement of all epiphyses. Pelvis not indented. Marked bow legs due to both genu varum and bowing of the tibiae.

Blood, urine and faeces nil abnormal. Radiographs showed active rickety changes. Calcium excretion was found to be definitely low when she was ten years of age; later estimates varied considerably. The serum calcium at that time was 10·4 milligrams per 100 cubic centimetres and the plasma phosphorus was 3·6 milligrams. Alkaline phosphatase raised (25 units).

In spite of careful treatment throughout the healing of the rachitic changes was very slow and when seen in 1949 at nearly fifteen years the legs were still markedly bowed, and she waddled badly. Height considerably below normal. Radiographs showed the epiphysial line changes almost cured and the bones generally improved in strength. Operative treatment of the bow legs was decided upon. (Under Mr A. O. Parker and Dr A. G. Watkins.)

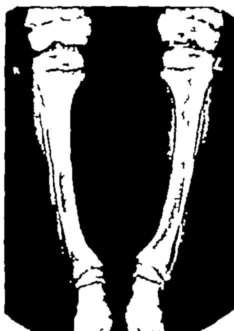


FIG. 339

Case 116—Legs (1941) at age of six and three-quarters years, showing rickety changes at all the epiphyseal lines, and rather poor texture of the bones generally.



FIG. 340

Case 116—Wrist (1945) at age of eleven years, showing rickety changes at lower ends of radius and ulna still active.



FIG. 341

Case 116—Same wrist (1949) at age of nearly fifteen years, showing considerable improvement but the epiphyseal changes still not quite healed.

CASE 117—RESISTANT RICKETS

(Figs. 342 to 345) R. G female aged six years. In 1937 said to have had signs of rickets for past two years only Intensive treatment proved unsuccessful. Typical rickets with enlarged epiphyses beading of ribs, Harrison s sulcus, and bowing of tibiae Urine normal Blood examination urea normal serum calcium 11 3 milligrams per 100 cubic centimetres. Fats in dried faeces 45 to 55 per cent. Radiographs revealed active rickets Lines of arrested growth well seen in region of knee joint Case was regarded as one of coeliac rickets and treated as such without success. Re-investigation fourteen months later showed no excess of fats in the dried faeces and the diagnosis of coeliac disease was abandoned and replaced by one of resistant rickets. When seen at age of eleven years and again at fourteen years, the rickets was still unhealed in spite of vigorous treatment Serum calcium was then 9 milligrams and the plasma phosphorus 1 8 milligrams per 100 cubic centimetres. The daily dose of vitamin D was increased up to ten times the usual. (Under the late Sir Henry Gauvain)

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Fig 342
Case 117—Wrists t six years, showing intense rickety changes in the radius and ulna

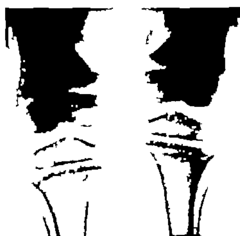


Fig. 343
Case 117—Knees t six years, showing hypocalcification active rickety changes at the epiphyseal lines, and "lines of arrested growth in femora and tibiae



Fig 344
Case 117—Pelvis and hips at fourteen years, showing rickety changes still not healed, and coxa vara on the left side

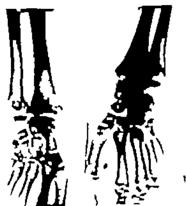


Fig. 345
Case 117—Wrists t fourteen years, showing rickety changes in the radius and ulna still active.

√

CASE 118—CONTINUED RICKETS



(Figs. 346 to 348.) E. C., female, aged eleven years. Knees began to swell when three years old. Within a year legs became bent and painful at times, usually at night. Six months ago wrists and ankles began to swell. Child obviously had not been cared for properly and almost certainly had never received adequate treatment. Child below normal in height and presents rickety deformities. Beading of ribs. Harrison's sulcus. Chest: some pigeon breast deformity. Epiphyses much enlarged. Tibiae curved and slightly tender. Feet valgoid. No evidence of renal or coeliac disease. Vigorous anti-rachitic treatment was successful in curing the rickets, which hardly deserved to be called "resistant." A sister, aged eight years, also has obvious signs of old rickets now almost cured.

Fig. 346

Case 118—Photograph of child, aged eleven years, showing enlarged epiphyses and deformities of the legs.



Fig. 347

Case 118—Arm at eleven years, showing active rickety changes at the wrist.



Fig. 348

Case 118—Legs showing the texture of the bones and active rickety changes at the epiphyseal lines.

CASE 119—CONTINUED RICKETS

(Fig 349 to 351) A. P boy aged six and a half years. A twin the other also has rickets but only in a mild form and without dwarfing Has never walked, and is only comfortable when lying down. Failed to grow normally Always languid and pale With the exception of frequent colds no definite illness. On admission he was deformed and dwarfed Head large square and bossed. Marked beading of ribs kyphosis and some scoliosis. Epiphyses very large General muscular hypotonia and laxity of joints including the metacarpo-phalangeal joints. Blood anaemia. Radiographs showed gross generalised hypocalcification, rickety changes in the metaphyses and at least a dozen fractures. No bowing of shafts except as a result of fracture. This case was seen with Dr F Langmead who reported it (Proceedings of the Royal Society of Medicine 1920 14 Section of Diseases of Children p 21) When the case was shown the possibility of osteogenesis imperfecta being present in addition to rickets was suggested but this received little support.



FIG. 349

Case 119—Photo of patient, with his twin sister showing the degree of dwarfing and the shape of his head.



FIG 350

Case 119—Arms showing the extremely porotic bones, rickety changes in the metaphyses and several fractures with unusually broad cracks.



Fig. 251

Case 119—Pelvis and legs showing gross hypocalcification, enlarged epiphyses with rickety changes, and fractures.

CHAPTER 28

LATE RICKETS

Late rickets a very uncommon disease in this country may be described as rickets in which the onset is delayed till later childhood or adolescence and at the earliest begins after the age of five years. It is to be distinguished from continued or resistant rickets in which the onset is before the age of four or five years. Some cases of late rickets however have had rickets, successfully treated in infancy so in these cases the new development may be regarded as a relapse. Some cases of late rickets are resistant to treatment. The older cases if not cured when growth ceases become cases of osteomalacia, and may be indistinguishable from cases of acquired raised resistance to vitamin D described by McCance (1947) In 1906 Elmslie collected thirteen cases from the literature and added three more. In the East it is far more common than in this country females being almost exclusively the victims In India it is chiefly seen in girls of the better class families soon after they adopt purdah and without obvious change of diet (Hutchison and Shah 1921-2) The girls of the poorer class families do not go into seclusion and therefore usually escape rickets. In China cases of late rickets frequently pass into a state of osteomalacia when growth ceases (Maxwell 1935) As a result of the hunger blockade of Prussia—and the same appears to be true of Austria and Japan—there developed during the year or two before and after the end of the first world war a number of cases of late rickets in addition to many of the infantile type In Prussia adolescents between the ages of fourteen and nineteen years were affected, the disease seldom being seen between six and fourteen years and curiously enough it occurred most often in males The reason for this was that the young males had to work hard and this involved much walking, standing for many hours a day and carrying heavy burdens, from all of which most young females were excused (Beninde 1920) In the more severe cases spontaneous fractures occurred.

Hereditary and familial influences—More than one member of a family may be affected and there may be a familial tendency to intrinsic resistance to vitamin D (Albright *et al* 1937)

Sex—Females are affected nearly twice as commonly as males.

Age—In our small series of twenty four published and unpublished cases the age of onset varied from five to eighteen years in fourteen the disease began after the age of ten years. This age incidence agrees with one of the springing up periods of Harris (1933)

Etiology—The cause is the same as in other types of rickets but in some cases the disease may be due to acquired raised resistance to vitamin D The onset may be precipitated by an illness such as an attack of gastro-enteritis (Evans 1923)

Clinical signs and symptoms—The sufferers often complain of fatigue and of pain in the back and hips. In the Indian cases pain was particularly complained of in the knee joints and later in the pelvis and spine It was slowly progressive but rarely was as bad as in osteomalacia (Hutchison and Stapleton 1924) The epiphyses may be tender In these late cases the usual rachitic deformities are seen but chiefly in the legs the head remains normal. They are usually rather short but not necessarily dwarfed. There may be some degree of sexual infantilism A rickety rosary and enlargement of the epiphyses at the wrists and knees, in addition to bowing of the tibiae may be seen Cases of continued and late rickets are said to develop secondary parathyroid hyperplasia occasionally like the infantile variety Linder and Vadas (1931) reported the removal of one enlarged parathyroid in a lad of nineteen years suffering from late rickets which had begun at seventeen

Blood Examination shows the same percentages of calcium phosphorus and phosphatase as in infantile rickets

Radiographic appearances—Films show changes typical of rickets at the epiphysial lines The pelvis may become funnel-shaped General hypocalcification may be present to a varying degree and is inclined to be more marked than in infantile rickets (Snapper 1949) Digital markings have been seen in the skull in one or two cases even in adolescence An "exostosis" as in other types of rickets, may be seen projecting from the inner side of the upper end of the tibia and this feature may or may not be symmetrical In severe cases multiple fractures not of the Looser zone type as a rule may be seen Multiple partial fractures may occur

Progress—Some cases resist large doses of vitamin D Relapse may occur Whether treated or not the rachitic changes disappear when growth ceases but if untreated or treated unsuccessfully the bones remain hypocalcified and the sufferer becomes a case of osteomalacia. The union of the epiphyses to the shaft may however be delayed.

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CASE 120—LATE RICKETS

(Fig 352) D B girl aged sixteen years. Said to have walked badly only during the past two years. At times can hardly walk at all. Gait rolling Epiphyses enlarged the wrists being quite typical Bow legs increasing in severity Radiographs showed only a suspicion of rickety changes which are practically healed in the femora and tibiae near the knee joints, but typical changes still active at the wrists. Lines of arrested growth were conspicuous at the lower ends of the femoral shafts and less so in the tibiae

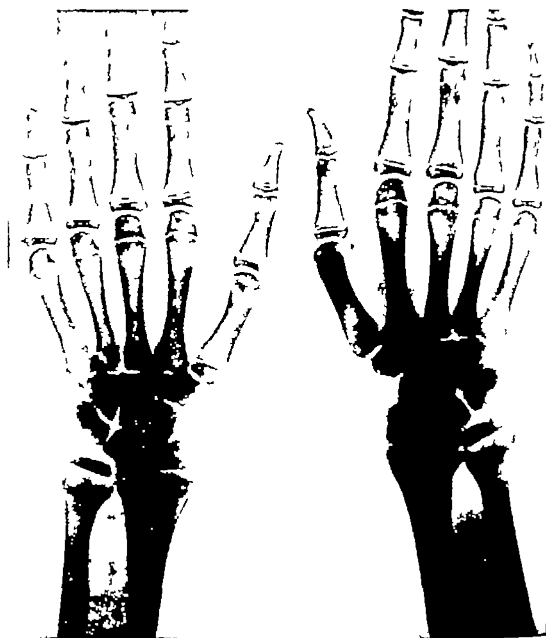


Fig 352

Case 120—Wrists and hands showing active rickety changes in the radius and ulna at the age of sixteen years.

CHAPTER 29

COELIAC RICKETS

This condition is true rickets occurring in children suffering from coeliac disease which is characterised by difficulty in the absorption of fats. The chief distinguishing feature of this type of rickets is the excess of fat in the stools which in all but the milder cases are large pale loose and offensive The original description of this nutritional disease we owe to Gee (1888) Valuable reviews of the subject were published by Parsons (1927 1931) and May (1947)

Hereditary and familial influences—Seldom has more than one case occurred in a family Corner (1940) reported twins affected with coeliac disease

Sex—Girls are more frequently affected than boys

Age—It commences most frequently in infancy from the ninth month to the end of the second year but is often not diagnosed till some years later (Parsons 1931) not infrequently about the sixth year We have seen a lad of eighteen years with signs of active rickets as well as general hypocalcification of the skeleton both the result of coeliac disease which had been present for at least seven years.

Etiology—The exact cause is unknown There is no enteritis. The skeletal changes are usually attributed to the failure to absorb vitamin D calcium and phosphorus in normal amounts from the bowel. In 1948 Sheldon gave reasons for regarding starch intolerance in children with coeliac disease as perhaps of greater etiological importance than the well-known failure to absorb the products of fat digestion and in 1949 he reported further work on these lines

Signs and symptoms—The onset is insidious usually with digestive symptoms. Diarrhoea is common but may be absent in the less severe cases. The stools are large pale and offensive and contain an excess of fat the amount varying from time to time The percentage of fat in the dried stools is increased to anything from 40 to 80 per cent —normal 25 per cent — (Parsons 1931) The abdomen is distended The liver is small a point regarded as of some diagnostic importance by Still (1918) There is wasting muscular hypotonia particularly in the legs and failure to gain weight at the normal rate Skeletal changes except for some hypocalcification and minor deformities usually develop late perhaps not for a few years but they may appear in infancy if the disease is sufficiently severe Stunting of growth is usual and not uncommonly the degree of dwarfism is extreme this is due to retardation of growth and not to premature fusion of epiphyses. The dwarfism is inclined to be of the short limbed type Infantilism may be present but not invariably secondary sex signs may be delayed until the twentieth year or even later Growth is of course essential for the development of rickety changes if such changes have occurred in infancy they may disappear as the disease increases in severity and reappear at about the fifth or sixth year when growth returns (Parsons 1931) Anorexia is common and the child s general behaviour may show marked changes with irritability fretfulness capriciousness and reluctance to smile The mental attitude may vary with the activity or quiescence of the diarrhoea. Gluteal wasting as a sign of some value was stressed by Miller (1947) Dentition may be delayed and the enamel of the teeth defective In a case with fully developed rachitic changes the epiphyses are enlarged and the limbs may be tender the latter possibly due to the presence of a scorbutic element The knee jerks may be absent Deficiency symptoms that may be present in addition to diminished growth and bone tenderness are oedema free fluid in the abdomen and xerophthalmia the last only very seldom (Parsons 1931)

Blood examination—Secondary anaemia is common. The serum calcium is low and the plasma phosphorus either low or normal. The alkaline phosphatase is usually but not invariably raised. The blood sugar curve is low and flat.

Radiological appearances—There is generalised hypocalcification of the skeleton with or without the changes characteristic of rickets. Subnormal density may be the only skeletal change for long periods. The degree of hypocalcification and thinning of the cortex are greater than in ordinary rickets and when rachitic changes are absent the translucency of the bones is most striking (May 1047). Occasionally the metaphyses and adjacent portions of the shafts may be honeycombed and almost cystic in appearance as they are sometimes in osteogenesis imperfecta. In some cases longitudinal striation is seen. The rickety changes at the epiphysial discs when present usually differ in no way from those seen in ordinary rickets. As examples of the variability of the skeletal changes may be mentioned a girl of nine years with general hypocalcification only and a lad of eighteen and a half years with rachitic changes in addition to deficient calcification of all the bones. Both the commencement of ossification of the epiphyses and their fusion to the shafts may be delayed, making it possible for rachitic changes to be seen well beyond the age of twenty years. We have seen one striking exception in which premature fusion appeared to be taking place. Lines of arrested growth in the long bones are often a noticeable feature and indicate the effect on skeletal growth of the irregular course of the disease. Coxa vara and other deformities may be seen. In the majority of cases the active rickety changes are cured by appropriate treatment.

Progress—Published statistics differ considerably with regard to the mortality rate while Sheldon (1048) estimates the mortality from various causes as at least 10 per cent., some authors report a much higher percentage. New methods of treatment seem likely to improve the outlook. Only occasionally does the disease continue into adult life but in the majority *of cases of so-called idiopathic steatorrhoea in adults admittedly an uncommon affection*, the disease can be traced back to childhood. In one woman aged fifty five years, with idiopathic steatorrhoea the disease started at the age of ten years (Konstam 1036). For some years after cure is apparently complete the cases are often abnormally fat and suggestive of Frohlich's syndrome. The majority can never attain a normal stature.

Complications—Since the serum calcium is usually low tetany is not infrequent. Other complications due to deficiencies that have been met with are scurvy pellagra beri-beri glossitis and haemorrhage from the bowel the last being due to lack of vitamin K (May 1947). Multiple fractures may be present and in some cases the width of the pseudo-fractures and the absence of visible callus are strongly suggestive of Looser's zones and may warrant a case being labelled as one of Milkman's syndrome this is more frequently met with in the older patients.

Pathology—The only notable finding in the bowel is an absence of enteritis. The skeletal changes are similar to those of rickets.

Diagnosis—Diagnosis is not difficult provided coeliac disease is not forgotten and the stools are examined in every possible case. It is the cases of hypocalcification and rickety changes at ages beyond those at which infantile rickets is common that call for thorough investigation to exclude or confirm a suspicion of possible coeliac or renal disease. Even when the presence of steatorrhoea is proved certain causes other than coeliac disease have to be excluded these include tubercular abdominal glands certain infections including lamblia intestinalis, and fibrocystic disease of the pa¯¯eas. The diagnosis is discussed fully by Sheldon (1948). Symptoms of fibrocystic dise … ncreas are present at birth and this affection shows a greater familial tendency … disease. Generalised osteoporosis without rachitic changes … used by hy … oidism but this is very seldom met with in children, and it … ot a fall … t of … ium in the blood.

IDIOPATHIC STEATORRHOEA

This uncommon disease in adults corresponds to coeliac disease in children. It is sometimes called Gee-Thaysen disease, Gee having described coeliac rickets in 1888 and Thaysen the same affection in adults in 1930 and 1932. No definite line can be drawn between the disease in childhood and that seen later in life; in fact the majority, though not all, of the adult cases can be traced back to childhood (Tidy 1940; Hunter 1940). Tidy gives a good résumé of the subject. It is a nutritional disease characterised by fatty stools, dilatation of the colon, osteomalacia, anaemia, tetany and skin lesions.

Hereditary and familial influences—As in coeliac disease, there is little evidence of these.

Sex—Females are affected rather more commonly than males.

Age—The ages at which cases have been reported vary enormously. Bennett *et al.* (1932) published fifteen cases varying in age from fifteen to fifty-eight years; they included six cases under twenty years and three over fifty years, in one of whom the disease began at fifty-two. Konstam (1930) reported a woman of fifty-five years in whom the disease began at the age of ten years. Other examples of cases commencing in adult life are those reported by Nussbrecher and Morton (1937), a woman of forty years, and by Pearson (1944), a woman of thirty-nine years; in both these cases the disease began at the age of thirty-three years.

Etiology—The cause is unknown. The exact relationship to tropical sprue is still a matter of uncertainty.

Signs and symptoms—In those in whom the disease began in childhood varying degrees of dwarfism and infantilism are present. Diarrhoea is not as common a complaint in adults as it is in children suffering from coeliac disease; in fact there may be constipation. The faeces contain an abnormal amount of fat, amounting to as much as 80 per cent. of the dried faeces. The stools are foul and may be frothy and slimy. Irregular attacks of pyrexia and abdominal disturbance may occur. There may be enlargement of the colon and distension of the abdomen. The tongue is smooth. Anaemia is present in some cases. Pain in the bones and deformities, *e.g.* genu valgum and kypho-scoliosis, may be complained of. Clubbing of the fingers, opacities in the lens and skin lesions are seen in some. Spontaneous fractures may occur.

Blood Examination—The serum calcium is low; the plasma phosphorus varies and though commonly normal in amount it may be either high or low. The excretion of calcium in the stools is high, in the urine low. A flat blood sugar curve is said to be typical (Nassim and Martin 1940).

Radiological appearances—There is general hypocalcification of the bones with great reduction in the thickness of the cortices. As a rule there are many lines of arrested growth, indicating the fluctuating course of the disease after an early onset. There is a tendency to striation of the translucent bones, the trabeculae being mostly in the line of the shaft. The vertebral bodies are biconcave as in other cases of osteomalacia. There may be rarefied areas in the skull with multiple ill-defined rounded islands of varying density (Brailsford 1943). The pelvis may be indented. In the younger adults, in whom the disease began in childhood, epiphysial fusion may be delayed and active rickety changes may be present later than one would expect. In a young man of twenty-eight years reported by O'Sullivan and Moore (1941) union of several of the epiphyses had either not commenced at all or was incomplete. Though the onset was said to have occurred only some months before admission, infantilism was present and also moderate general hypocalcification of the skeleton. This man grew nearly an inch after treatment was commenced. In one case fusion of the epiphyses appeared to have been hastened rather than delayed.

Progress—Under appropriate treatment the bone changes can be arrested, and recalcification of the skeleton may occur but there is some difference of opinion as to the frequency of such success.

Complications—Tetany is often seen though not infrequently latent it is active in as many as 70 per cent. of the cases (Hunter 1946) Multiple symmetrical spontaneous fractures (Milkman's syndrome) may occur In three of the twelve cases referred to by Professor Moore (O'Sullivan and Moore 1941) multiple fractures occurred but they united satisfactorily when the disease was successfully treated. In thirty four cases of Milkman's syndrome reviewed by us idiopathic steatorrhoea was the underlying cause in three. Occasionally the fractures have been incomplete.

Pathology—The bone changes are those of osteomalacia with abundance of osteoid (Bennett *et al* 1932)

Diagnosis—In cases of osteomalacia the possibility of steatorrhoea being the cause must never be forgotten though there may be nothing suggestive in the history the faeces should always be examined. Generalised hyperparathyroidism is excluded by the fact that the serum calcium is low not high and by the presence of the special features associated with steatorrhoea.

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CASE 121—COELIAC DISEASE with general osteoporosis

(Figs. 353 and 354.) F. S., girl aged nine years. Admitted for severe genu valgum. Had been under treatment for coeliac disease for past two years. Said to have had marked rickets changes at one time and very offensive stool. A fat child with very large abdomen and marked genu valgum. Epiphyses not enlarged. Radiograph showed osteoporosis of the skeleton without active rachitic changes at the epiphysial lines. The genu valgum was dealt with later by osteotomy of the femora. No signs of coeliac disease on admission but later the stools became profuse, unformed and light coloured. Before discharge the stools were much more normal. (Under the late Sir Henry Gauvain.)

Fig. 353



Case 121—Knees showing general osteoporosis, thin cortices, imperfect modelling of the shafts of the femora and tibiae and no rachitic changes. Note the slight protuberance on the inner side of both tibiae in their upper third at the site at which exostoses are occasionally seen in various types of rickets.



Fig. 354

Case 121—Photo showing the large abdomen and the deformity of the legs.

CASE 122—COELIAC DISEASE with active rickety changes, dwarfism and infantilism

(Figs. 355 and 356.) P M male aged eighteen and a half years. Been under treatment for coeliac disease for at least seven years. Worse since attack of influenza two months ago. For last two weeks able to walk only very short distance. All his bones ache on use or rough handling Three years ago had severe bleeding after tooth extraction and had to be transfused, and two years ago had nose bleeding so there appears to have been a lack of vitamin K. Looks fragile and young for age. Some enlargement of epiphyses. Malleoli tender on pressure. Height 4 feet 7 inches Genu valgum 5 inches. Flat feet. Abdomen not very large. Fat in dried faeces amounted to 40 per cent Radiographs showed general hypocalcification with signs of active rickets at the epiphyseal lines Longitudinal striation visible in the ends of the shafts of some bones. He improved considerably under more vigorous treatment. Grew three inches in twenty months, but was still far below normal height and the rachitic changes were still unhealed. (Under Dr Donald Paterson)



Fig. 355
Case 122—Hand showing the general hypocalcification with thin cortices and signs of active rickets in the radius and ulna



Fig. 356
Case 122 Knees showing hypocalcification with thin cortices of femoral and tibial shafts, longitudinal striation of the metaphyses and epiphyses, and signs of active rickets Note the transverse lines of arrested growth

CASE 123—COELIAC DISEASE with ACTIVE RICKETS

(Fig. 357.) P. M. boy aged eleven years. Known to have had coeliac disease for at least eight years. Genu valgum. Radiographs showed general hypocalcification and active rickets. Lines of arrested growth particularly well seen.

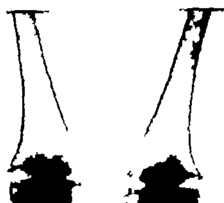


FIG. 357

Case 123—Femora showing the thin cortices of the shafts, rickety changes at the epiphyseal discs and lines of arrested growth. Note the line situated a considerable distance from the distal end of each femoral shaft: possibly this corresponds to the onset of the disease. Similar lines were seen in the upper third of the tibiae.

CASE 124—COELIAC DISEASE

(Figs. 358 and 359.) P. F. female aged seventeen and a half years. Trouble with feeding at six months of age and later developed rickets and was under the care of the late Sir Frederick Still. Began walking when five years old and then bones began to bend. After walking for eighteen months she was taken off her feet and has hardly walked at all since except for a time on crutches. Family of six: one had rickets and died of whooping cough. A pale dwarf with legs particularly short. Right genu varum due to marked deformity of tibia. Right leg two and a half inches shorter than left. Mild scoliosis. Radiographs showed skeleton of normal density, epiphyses large compared with shafts, to which they are completely united. Operative correction of deformity of right leg was carried out. Twenty-three years later when a woman of forty years she was reported to be working as a missionary in India. Films taken when she was seven years old showed curious irregular increased density about the central portions of the epiphyseal lines at the lower end of the femur and upper end of the tibia respectively.



FIG. 358

Case 124—Right knee at age of seven years, showing the curious irregular density at the central portions of the epiphyseal lines of the femur and tibia. In the femur premature fusion of the epiphyses appears to be occurring. Note the displacement of the head of the fibula.



FIG. 359

Case 124—Right knee at age of seventeen years showing complete fusion of the epiphyses, marked deformity of the tibia and fibula, and further displacement of the fibular head.

CHAPTER 30

OSTEOMALACIA

This affection of adults corresponds to rickets in children and is due to similar causes. It is a relatively uncommon disease in this country but is much more often met with in the East, where it is not infrequently preceded by late rickets. In idiopathic steatorrhoea the changes in the skeleton are identical with those of osteomalacia.

Hereditary and familial influences do not affect the incidence of the condition in this country. In the East the mode of life responsible for the disease is followed by every female member of a family and all are prone to develop it.

Sex—Females are far more commonly affected than males but not exclusively.

Age—It may occur at any age after growth has ceased the actual date of onset depending on the cause. If due to exceptional resistance to vitamin D the sufferer is a young adult. In such cases the condition may be the immediate successor of late rickets. In China most of the cases are young women (Maxwell 1934). When hunger osteopathies were prevalent in Germany and Austria after the first world war women of forty to sixty years, especially if pregnant or at the puerperium formed the bulk of the sufferers, women of twenty to thirty-five years seldom being affected (Beninde 1920). In India it is seen mostly in the young women of the better class families in which the females either practise strict purdah or rarely go out of doors (Hutchison and Stapleton 1924) and it may be preceded by late rickets.

Etiology—The cause is deficiency of vitamin D and calcium, due either to dietetic errors, lack of sunlight or occasionally to an acquired abnormal resistance to vitamin D as in the case reported by McCance (1947). No longer are the ovaries regarded as responsible, though pregnancy and lactation, which involve additional heavy calls on a woman's vitamins and calcium may be aggravating causes which in some cases are recurrent. The fact that the disease occasionally attacks males puts the ovaries out of court. In diabetics long continued acidosis may lead to osteomalacia (Lawrence 1948). Hepatic cirrhosis has also been associated with osteomalacia (Ask Upmark 1939).

Signs and symptoms—Pain is a frequent early symptom the sites most commonly affected being the lower back pelvic region, thighs and occasionally the ribs. The gait becomes waddling. In advanced cases the sufferer is unable to walk and may even be afraid to move or be touched on account of the pain produced by the slightest activity. The long bones become curved. The sternum may be bent. Some degree of spinal and thoracic deformity may develop. In the spine kyphosis is common and is often combined with lordosis below the latter being chiefly the result of the forward displacement and tilting of the sacrum. Increasing muscular weakness is the natural result of the inactivity. Approximation of the costal margin to the iliac crest with the production of transverse folds of the skin is regarded as characteristic by Meulengracht (1939).

Blood Examination as a rule reveals rather subnormal amounts of serum calcium low plasma phosphorus and raised alkaline phosphatase. The calcium balance is usually negative.

Radiological appearances—There is generalised hypocalcification of the whole skeleton. The density of the bones is much diminished, with the cortices either finely laminated or reduced to delicate lines. The normal curves of the bones are increased and abnormal curves appear with or without antecedent fractures. The pelvis is indented and triradiate making normal childbirth impossible in many cases. The pubic arch is narrow. The vertebral bodies are biconcave and the intervertebral discs biconvex. The tilt of the sacrum is increased, nearly to a horizontal position and it is folded on itself. The skull may be of uneven density with multiple fairly clear cut areas of translucency (Hunter 1948). Maxwell (1930) in the

has repeatedly found the pelvis and chest affected without the long bones showing appreciable changes If the long bones were affected the chest and pelvis rarely escaped

Complications—The two chief complications are fractures which may occur spontaneously in bed and tetany Osteomalacia is the usual underlying cause of the condition now commonly known as Milkman's syndrome in which multiple symmetrical spontaneous fractures occur Fractures may occur in several of the metacarpals and metatarsals Tetany is now uncommon but apparently the frequency varies with the country in which the cases occur In China at least 1 per cent of the severe cases develop cataract—cataracta tetanica—according to Maxwell and Pi (1940) but we have not seen this complication reported in this country The changes in the eyes are not conspicuous and require specially looking for Swelling of the thyroid is said to be common in nutritional osteomalacia (Kienboeck 1939) Snapper 1949)

Pathology—The chief feature in any bone examined besides a reduction in the amount of properly ossified matrix is the abundance of poorly calcified osteoid of which exceptionally wide seams cover the trabeculae or even entirely replace them In the marrow there is considerable hyperplasia of connective tissue and a fibrillated tissue is formed, which in places merges into the osteoid tissue (Muir 1941) Though never sufficient to deserve the name of osteitis fibrosa the amount of fibrous tissue formed apparently depends on the rapidity with which the decalcification occurs (Jaffe *et al* 1932) The degree of absorption of the trabeculae is far more severe than in disuse atrophy while in addition the cortices are thinned (Harris 1933) The magnesium content of the bones is said to be increased. Secondary enlargement of the parathyroid has been reported in a few cases but without signs of hyperparathyroidism (Snapper 1949)

Diagnosis—Cases of hypocalcification secondary to idiopathic steatorrhoea must be excluded by estimation of the amount of fat in the dried faeces and those due to renal osteo-dystrophy by examination of the urine and blood. Hyperparathyroidism is excluded by the absence of increase in the serum calcium. In senile osteoporosis the spine is the particular site affected by osteoporotic changes Thyrotoxic osteoporosis should be recognised without difficulty tenderness of the bones may be present and this but not always the osteoporosis can be relieved by thyroidectomy Diabetes should always be excluded by examination of the urine Cushing's syndrome which may also be associated with osteoporosis is distinguished by virilism in females—feminism in males—adiposity hypertrichosis and frequently diabetes mellitus. General osteoporosis may also be seen in Simmonds disease and may result from long continued recumbency from any cause particularly when associated with cachexia.

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CHAPTER 31

MILKMAN S SYNDROME

This is a condition characterised by the presence of multiple spontaneous idiopathic symmetrical fractures and described by Milkman in 1930 and 1934 As others have pointed out including McCullough (1940) and McCance (1947) this is not a disease but a clinical description of a condition revealed by radiological examination and which may be met with whenever the skeleton has become sufficiently hypocalcified It has occurred particularly in association with osteomalacia including the so-called puerperal cases and the hunger osteopathies but also in coeliac disease and idiopathic steatorrhoea and occasionally even in very severe rickets including cases of the resistant continued and late types and in what McCance has called acquired R R.D (raised resistance to vitamin D) In 1920 Looser in reporting a variety of cases suffering from hunger osteopathies described certain multiple lesions in the bones which he regarded as pseudo-fractures and which he called umbauzonen, or transformation zones these are now often spoken of as Looser s zones or bands. Milkman reported his case with multiple pseudo-fractures in 1930 and the same case formed the basis of the syndrome he described in 1934 In 1932 Michaelis had reported a case of the same type in which the condition had begun when the patient was a lad of eighteen years. In 1937 Leedham-Green and Golding reported a case and suggested the title osteoporosis melolytica or meloclastica for the syndrome. We hesitate to accept either of these titles since although the majority of the local lesions may certainly be found in the limb bones an important feature of the condition besides the unique appearance of at least some of the lesions is, in our opinion that the pseudo-fractures are seen also in the pelvis and scapulae sites seldom if ever affected by spontaneous fractures except in the presence of a cyst or neoplasm. The skull also may show changes. The mere occurrence of multiple spontaneous fractures is not sufficient to place a case in the syndrome Multiple fractures occur more or less spontaneously in osteogenesis imperfecta, hyperparathyroidism hyperthyroidism and polyostotic fibrous dysplasia, but the fractures seen in these affections have not the typical appearance of Looser s zones Multiple partial fractures may occur in Paget s disease and in some other conditions as yet unclassified but they are not as a rule symmetrical they do not affect the flat bones, and they are not really of the Looser zone type In senile osteoporosis the fractures are usually confined to the vertebral bodies. Some thirty four cases which have either been published as cases of Milkman s syndrome or appear to belong to this group have been studied Whether or not a particular case should be included may well be a matter of opinion In this author s opinion march fractures are the result of local muscular fatigue in one provided with but little margin of safety in the strength of his bones and have no similarity whatsoever to the fractures seen in this syndrome

Hereditary and familial influences appear to play no part in the incidence but the brother of a case reported by Macey (1940) with multiple pseudo-fractures was also found to have a few similar skeletal lesions.

Sex—Females are far more frequently affected. Only six males are included in the thirty-four cases studied

Age—The ages in this series ranged from eighteen to sixty two years. More than two-thirds were in the age group thirty to sixty and most of these were between thirty and forty The age at the time of onset of the skeletal disease in many of these cases is not recorded, but in two it began as early as the fifteenth year (Linder and Vadas 1931 McCance 1947) while in a third case the first complaint was as late as the fifty ninth year (Revault *et al* 1938) In a case of severe rickets with multiple fractures reported by Bevan (1937) a child of only two years the appearance of several of the fractures was very suggestive of Looser s zones

Etiology.—In most cases the cause is that of osteomalacia and this need not be considered here. In exceptional cases the generalised hypocalcification is associated with ordinary rickets. In three of our series it was due to steatorrhoea. It is not known why the particular lesions described by Looser should occur in some cases of general hypocalcification and fragility of the skeleton while in others any fractures that occur have no unusual features. In only three cases in this series does pregnancy seem to have played a part and in these no more than a secondary part in the incidence.

Signs and symptoms.—The onset is slow and insidious and some years may elapse—eight years in one case—before the typical clinical picture is fully developed. There may be periods of intermission and exacerbation. The sufferers complain of pains usually in the lower back and legs. Pain and even tenderness in a bone may occur before there is any radiographic evidence of a pseudo-fracture. On the other hand many of the "zones" revealed by X rays give rise to no local clinical signs. No crepitus is felt. Progressive weakness eventually renders the sufferer unable to walk and later necessitates confinement to bed. There are no diagnostic signs other than those provided by radiographic film and these as already indicated may be slow in making their appearance.

Blood Examination is much the same as in osteomalacia without fractures. Though usually about normal in amount the serum calcium may be low and tetany may occur. The plasma phosphorus is low. Little information is available with regard to the alkaline phosphatase but presumably it is usually raised as in ordinary osteomalacia. In a case due to steatorrhoea the alkaline phosphatase was raised but it fell progressively as recalcification occurred under treatment (Nassim and Martin 1940). In the man of thirty-six reported by Macey (1940) and already referred to there was no phosphatase at all in the plasma until a fractured femur was plated when it appeared in the blood for a few weeks and was then reduced to a mere trace; his brother also had a very low phosphatase reading. In one case seen a woman of forty-four the amounts of both the alkaline and acid phosphatase in the plasma were about normal.

Radiographic appearances.—There is generalised subnormal density of the bones associated with multiple fractures. Not only are these fractures or "pseudo-fractures" spontaneous and inclined to be symmetrical but many of them have special and distinctive features. In addition to the shafts of the long bones they are seen at sites which are seldom if ever affected by fractures except as a result of very definite trauma such as the rami of the pubis and ischium and the scapulae. Films showing symmetrical pseudo-fractures in these bones are particularly striking. In the scapula the fracture is incomplete usually showing as a dent, notch or crack in the axillary border of the bone. In a typical Looser's zone the clear band is not a mere line or crack, but is of considerable width, even as much as a centimetre. There is no visible callus and no sclerosis of the adjacent parts of the two fragments, or only very little. There is no displacement and none may occur even over a period of years. In the case reported by Milkman (1934) five years elapsed after X rays had revealed a lesion in a femur before the bone gave way. More than one zone may be seen in a bone particularly in a rib. The pubes, femora, upper thirds of the ulnae and the ribs are the most common sites. The minor long bones of the hands and feet may be traversed by pseudo-fractures. The zones are usually transverse but may lie obliquely or be zig-zag. When only partial the fractures appear as a notch or even a hole not a fine crack; they slowly progress across the bone. It is not essential that *every* lesion should have the typical Looser appearance; some may be just a fine crack—a linear fracture. *During the activity* of the disease presumably there must be some callus surrounding a pseudo-fracture and helping to prevent displacement though this is invisible. As soon as the osteomalacia responds to treatment provisional callus and sclerosis appear and consolidation of the fracture proceeds satisfactorily. In the skull may be seen many pale mottled areas or shadows up to a centimetre in width. Hunter and Turnbull (1931) publish a particularly striking radiograph showing the changes in the skull of an osteomalacic with multiple fractures. The areas of porosis in the skull may be

symmetrical. In some cases the appearance is not unlike myelomatosis. In the case reported by Michaelis (1932) myelomatosis was actually suspected until excluded by biopsy. In one case a coracoid process was affected (Lejeune 1946) and in another a patella. We have seen the manubrium sterni bent sharply backwards. Coxa vara with or without a local fracture may be present. As a rule the bones are not bent with the exception of the pelvis which may show deformity which is only partly the result of collapse resulting from the fractures. The number of pseudo-fractures present in a case may reach a high figure. There were forty three in Milkman's case and thirty nine in the case reported by Brick and Bunch (1947) in the latter case there were five fractures involving the vertebral bodies, several in the pedicles and spinous processes, and others in the manubrium sterni acromion processes, and one in the distal phalanx of a finger

In one or two cases showing typical pseudo-fractures the hypocalcification of the bones as seen in films was not as gross as one might have expected.

Progress—The condition slowly progresses if not checked by treatment there may be intermissions and exacerbations. Several reported cases improved markedly under treatment, and the fractures healed with no lack of callus (McCance 1947) The disappearance of the multiple lesions in the skull as a result of treatment is convincingly illustrated by Hunter and Turnbull (1931)

Complications—The only complication worthy of mention is the occurrence of one or more clinical fractures displacement having taken place at the site of a pseudo-fracture.

Pathology—Nothing special or instructive has been revealed by the limited number of microscopical investigations published. In the zones some increased vascularity has been found, with increased lacunar absorption as might have been expected. The marrow showed mostly fat and fibrous tissue Wettstein (1947) found some cartilage in the fibrous tissue. Gambier (1949) found plenty of osteoblasts and definite fibrosis in a zone The only constant finding has been abundance of osteoid in the bones clear evidence of osteomalacia. There seems to be general agreement that the condition is associated with no definite pathological picture.

Diagnosis—This depends on the radiographic appearances. The cause of the general porosity of the skeleton which forms the background of the syndrome should be disclosed by the usual investigations This is of far greater importance than the decision as to whether or not a particular case should be labelled one of Milkman's syndrome. Some of the cases with multiple partial fractures confined to a limited portion of the skeleton as in the case published by Curr (1948) await a satisfactory explanation and classification

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CASE 125—OSTEOMALACIA

(Figs. 300 and 301.) Female aged sixty years. Unmarried. Operation for genu valgum in adolescence. Genu valgum was only deformity noticed till she was twenty, when she had a severe illness which confined her to bed for twelve months. Has spent her time in a chair or in bed for many years. Sustained a fracture of left tibia some years ago and also of one humerus. Deformities have been increasing steadily for twenty years. Admitted to hospital for cataract. Marked scoliosis. Bowing of femora, humeri, right tibia and fibula and right radius. Sclerotics not blue. Radiographs showed marked generalised hypocalcification. Pelvis shows triradiate deformity.



FIG. 300
Case 125—Pelvis showing gross indentation.



FIG. 301
Case 125—Legs showing advanced hypocalcification and deformity of the left tibia and fibula.

CASE 126—OSTEOMALACIA WITH MILKMAN'S SYNDROME

(Figs. 362 and 363) Mrs F G aged forty-six years. Has had nine children the youngest born seven years ago all delivered naturally except the first for which instruments were used. Present trouble began eight and a half years ago when she was three or four months pregnant with the last but one child with pain and swelling of the feet. After delivery of this child she was slow in getting on to her feet but eventually recovered completely Trouble recurred during last pregnancy with pain and stiffness in her legs and spine. Has been obliged to use a stick ever since Is now losing the use of her hands which are inclined to swell when used. Pain in right shoulder Had bronchitis three months ago and since then has found legs shaky and has been unable to walk. Some pain in knees but none in spine now On examination oedema of feet and legs. Genu valgum but this has been present since age of twelve years. Knees not tender but were at one time. Trochanters on level with anterior superior spines. Attempts at adduction of legs cause pain Costal margins are below iliac crests. Hands white and clammy and suggestive of rheumatoid arthritis but there is no swelling of joints. Left first finger shows some deformity Wrist movements fairly good Some thickening of front of humeri at junction of middle and lower thirds. Left clavicle deformed Spine severe scoliosis and kyphosis. Radiographs show advanced general hypocalcification of the skeleton and typical pseudo-fractures (Looser's zones) in several bones particularly in those of the hands. Deformity of the left clavicle probably due to old fracture



Fig. 363

Case 126—pelvis and hips showing indentation with pseudo-fractures in the pubic and ischial rami



Fig. 303

Case 126—Hand showing a l[illegible] nced hypocalcification [illegible] ll the bones, with pseudo fract[illegible] res (Loose[illegible] zones) in sev[illegible] l phalanges and [illegible]ne metacarpal N[illegible]t the absence of [illegible] all [illegible] format[illegible]

CASE 127—OSTEOMALACIA WITH MILKMAN'S SYNDROME

(Figs. 364 to 368) H M male aged thirty-four years. Occupation miner In 1938 injured right leg Subsequently radiographed and found to have transverse fracture of tibia and fibula. Plaster fixation for long period followed eventually by bone grafting, but union did not occur Later complained of pain in left hip X rays showed a fracture of femoral neck. Neck explored in 1942 but no enlarged parathyroids found When transferred to present hospital in 1943 he had not walked since 1939 Complete biochemical investigation revealed nothing abnormal except a slightly lowered excretion of ascorbic acid which was corrected by full doses of vitamin C. Radiographic examination revealed generalised hypocalcification of the skeleton with typical pseudo-fractures in the upper thirds of both ulnae, both femora, right tibia and fibula and two lower ribs. Also old fractures seen in left femoral neck left fibula, and possibly horizontally across the left ilium There is varus deformity of the upper ends of both humeri. Pelvis shows little if any deformity Skull shows some irregular hypocalcification. The vertebral bodies are biconcave and porotic.

In spite of the pseudo-fractures still present in radiographs, in October 1943 he was able to walk with sticks, and complained of little pain Six months later though still getting about with sticks he had better control of legs and arms, but did not attempt stairs. (Under Mr E W Knowles.)



Fig 364

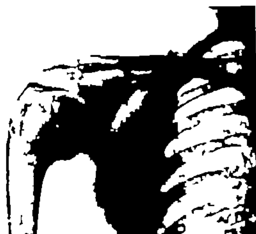
Case 127—Pelvis and upper femora showing hypocalcification slight narrowing of the pelvic inlet possible old fracture across the ilium above the acetabulum, an old fracture of the left femoral neck and pseudo-fracture in the subtrochanteric region of this femur



Fig. 365
Case 127—Right leg showing pseudo-fracture in the fibula nd t least tw partial fractures in the tibia.



Fig. 367
Case 127—Forearms showing typical symmetrical pseudo-fractures n the lnae



F g 368
Case 127—Right shoulder showing the deficient density f th bones and the varus deformity f the h merus.



Fig 369
Case 127—Spine showing hypocalcification of the vertebral bodies which are biconca the discs being biconvex

CASE 127—OSTEOMALACIA WITH MILKMAN'S SYNDROME

(Figs. 364 to 368.) H M male aged thirty four years. Occupation miner In 1938 injured right leg Subsequently radiographed and found to have transverse fracture of tibia and fibula. Plaster fixation for long period followed eventually by bone grafting but union did not occur Later complained of pain in left hip X-rays showed a fracture of femoral neck. Neck explored in 1942 but no enlarged parathyroids found. When transferred to present hospital in 1943 he had not walked since 1939 Complete biochemical investigation revealed nothing abnormal except a slightly lowered excretion of ascorbic acid which was corrected by full doses of vitamin C. Radiographic examination revealed generalised hypocalcification of the skeleton with typical pseudo-fractures in the upper thirds of both ulnae, both femora, right tibia and fibula, and two lower ribs. Also old fractures seen in left femoral neck left fibula, and possibly horizontally across the left ilium. There is varus deformity of the upper ends of both humeri. Pelvis shows little if any deformity Skull shows some irregular hypocalcification. The vertebral bodies are biconcave and porotic.

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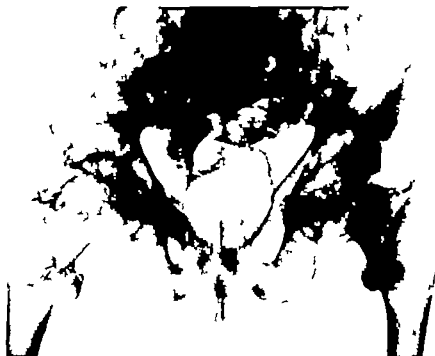


FIG 364

Case 127—Pelvis and upper femora showing hypocalcification slight narrowing of the pelvic inlet possible old fracture across the ilium above the acetabulum, an old fracture of the left femoral neck and a pseudo fracture in the subtrochanteric region of this femur



Fig. 365
Case 127—Right leg showing pseudo-fracture in the fibula and at least two partial fractures in the tibia.



Fig. 367
Case 127—Forearms showing typical symmetrical pseudo-fractures in the lnae

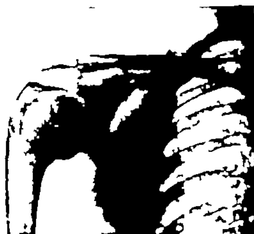


Fig. 368
Case 127—Right shoulder showing the deficient density f th bones and the varus deformity f the humerus



Fig. 368
Case 127—Spine showi g hypocalcification of the ertebral bodies which are biconcave th discs being bicon ex

CASE 127—OSTEOMALACIA WITH MILKMAN'S SYNDROME

(*Figs* 364 *to* 368.) H M male aged thirty four years. Occupation miner In 1938 injured right leg Subsequently radiographed and found to have transverse fracture of tibia and fibula Plaster fixation for long period, followed eventually by bone grafting, but union did not occur Later complained of pain in left hip X-rays showed a fracture of femoral neck. Neck explored in 1942 but no enlarged parathyroids found. When transferred to present hospital in 1943 he had not walked since 1939 Complete biochemical investigation revealed nothing abnormal except a slightly lowered excretion of ascorbic acid which was corrected by full doses of vitamin C. Radiographic examination revealed generalised hypocalcification of the skeleton with typical pseudo-fractures in the upper thirds of both ulnae, both femora right tibia and fibula, and two lower ribs. Also old fractures seen in left femoral neck, left fibula and possibly horizontally across the left ilium There is varus deformity of the upper ends of both humeri Pelvis shows little if any deformity Skull shows some irregular hypocalcification. The vertebral bodies are biconcave and porotic.

In spite of the pseudo-fractures still present in radiographs, in October 1943 he was able to walk with sticks, and complained of little pain. Six months later though still getting about with sticks he had better control of legs and arms, but did not attempt stairs. (Under Mr E W Knowles.)

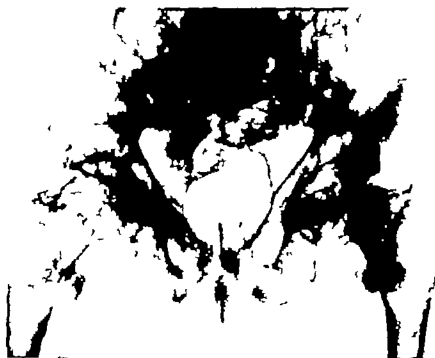


FIG. 364

Case 127—Pelvis and upper femora showing hypocalcification, slight narrowing of the pelvic inlet possible old fracture across the ilium above the acetabulum an old fracture of the left femoral neck and a pseudo-fracture in the subtrochanteric region of this femur



Fig. 365
Case 177—Right leg showing pseudo-fracture in the fibula nd t least two partial fractures in the tibia



Fig. 367
Case 127—Forearms showing typical ymmetrical pseudo-fractures in the ulnae

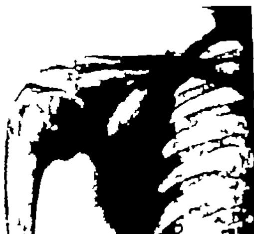


Fig 366
(se 127—Right shoulder showing the deficient lensit f the bones nd the varus deformity of the h merus



Fig. 368
Case 127—Spine showing hypocalcification of th vertebral bodies which re biconcave the discs being bicon x,

CHAPTER 32

RENAL OSTEO DYSTROPHY

Synonyms—Renal Rickets, Renal Dwarfism Renal Infantilism

In this condition general skeletal changes are associated with chronic renal deficiency which may either be the result of congenital anomalies of the kidneys or due to acquired nephritis. Attention was first called to the association of late rickets with albuminuria by Lucas in 1883. Dwarfism and infantilism in children suffering from renal disease have been recognised for many years, and at one time Renal Infantilism was a popular title for the condition. Parathyroid hypertrophy is so commonly present in these cases that some authors have preferred the title Renal Hyperparathyroidism or Renal Osteitis Fibrosa Cystica. Renal Osteo-dystrophy is favoured by Snapper (1949) and is adopted here since it does not imply that the skeletal changes are strictly comparable with those of ordinary rickets and it is equally applicable to the corresponding cases met with in adults. Though the changes seen at the epiphysial lines in some cases may resemble those of rickets, in typical cases there are definite and important differences as pointed out by Brockman (1927) Valuable papers have also been written by among others Barber (1926) Parsons (1927) and, on the radiographic changes, by Teall (1928)

Hereditary and familial influences—Congenital hypoplasia of the kidneys giving rise to osteo-dystrophy may certainly occur as a familial affection, while several examples of the familial occurrence of cases due to chronic nephritis are quoted by Mitchell (1930) In a family of eight children recorded by Graham and Hutchinson (1941) three and possibly four showed signs of renal dwarfism.

Sex—Both sexes are affected, with no material preponderance of either

Age—Recognisable skeletal changes may appear as early as six months and as late as seventeen years a common age is said to be seven years. Occasionally a case has been noticed to be unduly small even from birth. Deformity at the wrists and ankles was noted at birth in a case reported by Paterson (1921) Ellis and Evans (1933) found the average age for definite signs was nine and a half years in their series but many had had symptoms in early infancy

Etiology—There is still a considerable difference of opinion as to the cause but most authors support the idea that the kidney is primarily responsible for both the bone changes and the parathyroid hypertrophy The cases with congenital hypoplasia and cystic disease of the kidneys provide strong evidence in favour of this view Ureteric dilatation or other obstructive signs were present in no less than fourteen of twenty cases reviewed by Ellis and Evans (1933) Dwarfism and infantilism may be apparent before there are any striking changes in the bones, and therefore a primary endocrine error is favoured by some. The frequency of parathyroid hypertrophy has made some regard this as being as important as the changes in the kidneys, with or without possible overriding pituitary disorder as suggested by Chown (1936) The frequency of hyperparathyroidism in these cases is not known with accuracy but it is almost certainly present in most of the cases showing advanced skeletal changes. Fibrosis may however occur in the bones without hypertrophy of the parathyroids, and is attributed to the acidosis (Snapper 1949) Hunter (1948) points out that renal rickets is not due to deficiency of vitamin D but to disturbance of endogenous calcium and phosphorus metabolism which follows phosphorus retention. Those who regard the kidneys as responsible argue that phosphorus is excreted into the intestines where it combines with calcium and prevents absorption of the latter in normal amounts (Mitchell 1930) Price and Davie (1937) in a full discussion of the etiology suggest that renal rickets may be regarded as the common ground of overlap of hyperparathyroidism and renal disease Albright et al (1937) favour the kidney

theory and stress the point that parathyroid hypertrophy does not produce epiphysial bone changes. Enlargement of the parathyroids does not necessarily mean hyperfunctioning glands.

Signs and symptoms—Common early signs are failure to grow at the normal rate and the development of deformities particularly genu valgum. Abnormal thirst, polydipsia and polyuria may be present for years before any skeletal changes occur except retarded growth in some cases the bones may be unaffected till after puberty (Price and Davie 1937). In a typical well-developed case the child is a dwarf of the short limb type and the complexion is sallow earthy pigmented and unhealthy. The skin is dry the hair is sparse. In many the superior maxillae are prominent while the lower jaw is receding producing a facies which is regarded as characteristic by Price and Davie (1937). The epiphyses may be enlarged as in rickets though this change is not invariably symmetrical. Genu valgum and pes valgus are common. Bowing of the tibiae is much less often seen. In spite of an unhealthy appearance the child may feel surprisingly fit and well though liable at any time to develop uraemia especially after an operation such as osteotomy for correction of deformity. Mental development is normal. Some degree of infantilism is apparent in the appearance and voice delayed sexual development is common. We have observed complete cessation of growth during a period of two years in a child who died of uraemia about a year after the last examination. The peripheral vessels may be calcified and readily palpable—this was so in eight of twelve cases examined specially for this sign (Ellis and Evans 1933)—yet hypertension and cardiac hypertrophy are exceptional. The eyes usually show no abnormality but retinitis and optic atrophy have been reported. Renal pain is uncommon but calculi may occur.

In advanced cases abrupt deformities may be present in the juxta-epiphysial regions the epiphyses being displaced this is seen most frequently in the necks of the femora (coxa vara) the lower ends of the femora and tibiae respectively and at the wrists. One or more epiphyses may even be completely detached and mobile without causing the patient any discomfort though such cases are necessarily completely crippled. In a child of eight years the lower epiphyses of the radius and ulna in both wrists were freely mobile and remained so till death. Limitation of movement of certain joints *e.g.* hips and knees may be associated with gross bony changes, as occurred in two children reported by Paterson (1920 and 1921).

Urine—Albumin in small amounts is usually present but occasionally it is absent. Casts, pus and micro-organisms are found in some cases. The excretion of calcium and phosphorus in the urine is always diminished.

Blood Examination—There is hypochromic anaemia acidosis and marked lipaemia (Parsons 1927). The plasma phosphorus is always raised even to 10-15 milligrams per 100 cubic centimetres. The serum calcium is usually low or at least relatively low but occasionally it is slightly raised. The alkaline phosphatase may be high but this is of no significance. The blood urea is always high particularly before death and may amount to anything from 73 to 663 milligrams per 100 cubic centimetres (Ellis and Evans 1933).

Radiographic appearances—The changes are of two types (Teall 1928) 1) Rachitic and 2) the characteristic Woolly Type. In the *Rachitic Type* which combines the atrophic and florid types of Parsons (1927) the changes are neither characteristic nor diagnostic. The density of the bones is fairly normal though osteoporosis may be present. Deformities due to bending are usually absent. Rachitic like changes are seen at the ends of the shafts but the opposing surfaces of the epiphyses are smooth and clear (Snapper 1940). Temporary healing may take place with or without special treatment or as a result of cessation of growth. If growth has ceased for good the rachitic X ray changes cannot return. In at least some cases the bones seem rather denser than normal and appear to be chalky and structureless. The skull shows no change (Brailsford 1944). In the *Woolly Type* there is generalised osteoporosis. Only quite exceptionally is the decalcification in the shaft of a bone irregular and so intensified in certain areas as to suggest the presence of cysts (Fairbank 1939). The metaphyses are prolonged more than in rickets and are not typically splayed and cupped. They are stippled

RENAL OSTEO DYSTROPHY

Synonyms—Renal Rickets, Renal Dwarfism, Renal Infantilism

In this condition general skeletal changes are associated with chronic renal deficiency which may either be the result of congenital anomalies of the kidneys or due to acquired nephritis. Attention was first called to the association of late rickets with albuminuria by Lucas in 1883 Dwarfism and infantilism in children suffering from renal disease have been recognised for many years and at one time Renal Infantilism was a popular title for the condition. Parathyroid hypertrophy is so commonly present in these cases that some authors have preferred the title Renal Hyperparathyroidism or Renal Osteitis Fibrosa Cystica. Renal Osteo-dystrophy is favoured by Snapper (1940) and is adopted here since it does not imply that the skeletal changes are strictly comparable with those of ordinary rickets, and it is equally applicable to the corresponding cases met with in adults. Though the changes seen at the epiphysial lines in some cases may resemble those of rickets in typical cases there are definite and important differences, as pointed out by Brockman (1927) Valuable papers have also been written by among others Barber (1920) Parsons (1927) and on the radiographic changes by Teall (1928)

Hereditary and familial influences—Congenital hypoplasia of the kidneys giving rise to osteo-dystrophy may certainly occur as a familial affection while several examples of the familial occurrence of cases due to chronic nephritis are quoted by Mitchell (1930) In a family of eight children recorded by Graham and Hutchinson (1941) three and possibly four showed signs of renal dwarfism

Sex—Both sexes are affected, with no material preponderance of either

Age—Recognisable skeletal changes may appear as early as six months and as late as seventeen years a common age is said to be seven years. Occasionally a case has been noticed to be unduly small even from birth. Deformity at the wrists and ankles was noted at birth in a case reported by Paterson (1921) Ellis and Evans (1933) found the average age for definite signs was nine and a half years in their series but many had had symptoms in early infancy

Etiology—There is still a considerable difference of opinion as to the cause, but most authors support the idea that the kidney is primarily responsible for both the bone changes and the parathyroid hypertrophy The cases with congenital hypoplasia and cystic disease of the kidneys provide strong evidence in favour of this view Ureteric dilatation or other obstructive signs were present in no less than fourteen of twenty cases reviewed by Ellis and Evans (1933) Dwarfism and infantilism may be apparent before there are any striking changes in the bones, and therefore a primary endocrine error is favoured by some The frequency of parathyroid hypertrophy has made some regard this as being as important as the changes in the kidneys, with or without possible overriding pituitary disorder as suggested by Chown (1930) The frequency of hyperparathyroidism in these cases is not known with accuracy but it is almost certainly present in most of the cases showing advanced skeletal changes. Fibrosis may however occur in the bones without hypertrophy of the parathyroids, and is attributed to the acidosis (Snapper 1940) Hunter (1948) points out that renal rickets is not due to deficiency of vitamin D but to disturbance of endogenous calcium and phosphorus metabolism which follows phosphorus retention. Those who regard the kidneys as responsible argue that phosphorus is excreted into the intestines where it combines with calcium and prevents absorption of the latter in normal amounts (Mitchell 1930) Price and Davie (1937) in a full discussion of the etiology suggest that renal rickets may be regarded as the common ground of overlap of hyperparathyroidism and renal disease Albright *et al* (1937) favour the kidney

theory and stress the point that parathyroid hypertrophy does not produce epiphysial bone changes. Enlargement of the parathyroids does not necessarily mean hyperfunctioning glands

Signs and symptoms—Common early signs are failure to grow at the normal rate and the development of deformities particularly genu valgum Abnormal thirst polydipsia and polyuria may be present for years before any skeletal changes occur except retarded growth in some cases the bones may be unaffected till after puberty (Price and Davie 1037) In a typical well-developed case the child is a dwarf of the short limb type and the complexion is sallow earthy pigmented and unhealthy The skin is dry the hair is sparse In many the superior maxillae are prominent while the lower jaw is receding producing a facies which is regarded as characteristic by Price and Davie (1037) The epiphyses may be enlarged as in rickets though this change is not invariably symmetrical Genu valgum and pes valgus are common Bowing of the tibiae is much less often seen In spite of an unhealthy appearance the child may feel surprisingly fit and well though liable at any time to develop uraemia especially after an operation such as osteotomy for correction of deformity Mental development is normal Some degree of infantilism is apparent in the appearance and voice delayed sexual development is common We have observed complete cessation of growth during a period of two years in a child who died of uraemia about a year after the last examination The peripheral vessel may be calcified and readily palpable—this was so in eight of twelve cases examined specially for this sign (Ellis and Evans 1033)—yet hypertension and cardiac hypertrophy are exceptional The eyes usually show no abnormality but retinitis and optic atrophy have been reported. Renal pain is uncommon but calculi may occur

In advanced cases abrupt deformities may be present in the juxta-epiphysial regions the epiphyses being displaced this is seen most frequently in the necks of the femora (coxa vara) the lower ends of the femora and tibiae respectively and at the wrists One or more epiphyses may even be completely detached and mobile without causing the patient any discomfort though such cases are necessarily completely crippled. In a child of eight years the lower epiphyses of the radius and ulna in both wrists were freely mobile and remained so till death Limitation of movement of certain joints, *e.g.* hips and knees may be associated with gross bony changes as occurred in two children reported by Paterson (1020 and 1021)

Urine—Albumin in small amounts is usually present but occasionally it is absent. Casts pus and micro-organisms are found in some cases. The excretion of calcium and phosphorus in the urine is always diminished.

Blood Examination—There is hypochromic anaemia, acidosis and marked lipaemia (Parsons 1027) The plasma phosphorus is always raised, even to 10·15 milligrams per 100 cubic centimetres. The serum calcium is usually low or at least relatively low but occasionally it is slightly raised. The alkaline phosphatase may be high but this is of no significance The blood urea is always high particularly before death and may amount to anything from 73 to 603 milligrams per 100 cubic centimetres (Ellis and Evans 1033)

Radiographic appearances—The changes are of two types (Teall 1928) 1) Rachitic and 2) the characteristic Woolly Type In the *Rachitic Type* which combines the atrophic and florid types of Parsons (1927) the changes are neither characteristic nor diagnostic. The density of the bones is fairly normal though osteoporosis may be present Deformities due to bending are usually absent Rachitic like changes are seen at the ends of the shafts but the opposing surfaces of the epiphyses are smooth and clear (Snapper 1940) Temporary healing may take place with or without special treatment or as a result of cessation of growth If growth has ceased for good the rachitic X-ray changes cannot return In at least some cases the bones seem rather denser than normal and appear to be chalky and structureless. Th skull shows no change (Brailsford 1944) In the *Woolly Type* there is generalised osteoporosis. Only quite exceptionally is the decalcification in the shaft of a bone irregular and so intensified in certain areas as to suggest the presence of cysts (Fairbank 1030) The metaphyses are prolonged more than in rickets and are not typically splayed and cupped They are stippled

and there is a general woolly appearance of the ends of the shafts. Subperiosteal erosion of the cortex even for some distance from the epiphysial line, is seen. Some of the epiphyses will be found to be displaced and tilted from the line of the shaft. The slipping takes place either at the epiphysial line or perhaps more commonly as the result of an oblique juxta-epiphysial fracture or collapse of the metaphysis a triangular fragment of the metaphysis is displaced with the epiphysis to which it remains attached. Multiple pseudo-fractures are said to occur (Brailsford 1944) but this complication is extremely uncommon. The skull is thickened, with the outer table woolly in appearance and either finely or coarsely mottled in some cases it is honeycombed. Clear areas in addition to mottling, were seen in the skull of a lad of twenty years (Langmead and Orr 1933) The definition between the inner and outer tables may be lost. Sometimes the appearance approaches that seen in Paget's disease. Though death may occur while the bones show only rachitic changes there is no doubt that the woolly type is seen in the more advanced and severe cases. Even the woolly type may show some signs of healing but not in the most advanced cases. Almost certainly in these cases hyperactivity of the parathyroids is present (Price and Davie 1937) Delay in fusion of the epiphyses may be observed in those who live long enough. The changes in the bones are not infrequently asymmetrical and erratic in their distribution or severity Snapper (1949) reports periarticular calcification in a girl of only thirteen years. Occasionally calcification of arteries may be seen even in the fingers (Brailsford 1944) Interstitial calcification may also be seen in the kidneys (Capon 1933 Ellis 1935)

Progress—Temporary spontaneous improvement occurs in some cases while others improve with treatment but sooner or later they all die of uraemia. The average at death was nine years and nine months in the series reviewed by Howard (1938) who states that if obstruction is diagnosed early enough a fatal termination may be avoided. Though unquestionably anti-rachitic treatment has resulted in at least temporary healing of the rachitic bone changes in a few cases such treatment is condemned by Parsons (1927) as risky and worse than useless.

Complications—Tetany is regarded as infrequent by most authors, but not by all.

Pathology—Though changes at the epiphysial lines apparently similar to those seen in ordinary rickets may occur (Hunter 1930) in all advanced cases the changes resemble rickets only superficially if at all. This fact was first clearly demonstrated by Brockman in 1927 The chief distinguishing feature is the presence of fibrosis. Generalised osteoporosis may or may not be present. On microscopic section of the region of the growth disc instead of excessive proliferation of cartilage cells and abundant formation of osteoid tissue (as seen in ordinary rickets) with little if any fibrosis in the adjacent marrow spaces, in renal rickets there is a partial or complete failure of the normal proliferation of cartilage cells and an absence of proper cartilage columns the formation of bone is limited and that which has formed is being actively absorbed by osteoclasts the area which should be the seat of calcified cartilage and recently formed bone trabeculae is mostly occupied by fibrous tissue which extends into the adjacent marrow spaces, while the rest of the red marrow is completely fatty Islets of cartilage may however be found deep in the metaphyses The vascularity of the juxta-epiphysial region is increased. Osteoid is seldom found On the surface of the shafts fibrous tissue replaces bone which has been absorbed under the periosteum When the changes are advanced growth of the bones must have completely ceased. The marked weakening of the metaphyses leads to the collapse and displacement of the epiphyses already mentioned. As Brockman found, the epiphyses may be joined to the shaft only by fibrous tissue and periosteum Occasionally the fibrosis in the shaft of a long bone may be sufficiently complete in certain areas to be conspicuous in a radiograph In the skull the bone is soft and there is vascular overgrowth of bone spicules and fibrosis of the marrow

The kidneys show a variety of changes—congenital and familial aplasia congenital cystic changes obstruction of the urinary tract with dilatation of the ureters and hydronephrosis

advanced renal destruction and sclerosis with or without pyonephritis in addition chronic interstitial nephritis and la th the renal deficiency may occasionally follow acute nephritis. After puberty chronic glomerulonephritis and calculous pyonephritis may be found (Snapper 1949). In those with definite hyperparathyroidism interstitial or even intratubular calcification may occur in the kidneys associated with secondary inflammatory changes.

As regards the parathyroids, when these show changes the usual finding is hyperplasia of all four gland and only rarely is there enlargement of only one or two glands. The enlarged gland show mostly either chief cells or water-clear cells but there may be some increase of the oxyphil cells. The pituitary is normal.

Diagnosis—The diagnosis is not difficult provided the kidneys are kept in mind as possibly responsible for dwarfism and infantilism and full investigation is made of every case that appears to be suffering from continued or late rickets. The urine of every case of adolescent coxa vara (slipped epiphysis) should be examined and the examination repeated before any operative procedure is decided upon (Brailsford 1933). The general appearance and complexion of a well-developed case should suggest the correct diagnosis. Only in exceptional cases I the urine free from albumin in renal osteo-dystrophy but the possibility of this should not be forgotten. Primary hyperparathyroidism may occur in childhood but is distinctly uncommon in this condition the serum calcium is of course raised.

In Fanconi's syndrome with general decalcification and renal glycosuria the plasma phosphorus is reduced instead of increased in amount and other features may be present. We have met with two cases children of six and eleven years respectively and both showing marked clinical signs of Renal Rickets whose urine contained sugar in addition to albumin.

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CASE 128—RENAL OSTEO-DYSTROPHY

(Figs. 369 to 371) D H male. Admitted to hospital when seven years old said to have been crippled since two years of age and suspected of being a renal case Definitely dwarfed and undeveloped Mentally normal Slight genu valgum On abdominal examination slight tenderness over the kidneys. Readmitted when fourteen years old. Very thin boy dwarfed. Drowsiness headache and vomiting were noted. Genu valgum was now marked Blood urea 81 to 84 milligrams per 100 cubic centimetres. Radiographs showed wide epiphyseal discs with some irregularity of metaphyses and in certain bones cupping Decalcification of the bones though present not a striking feature Died of uraemia about a month later

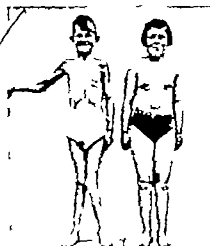


Fig. 369
Case 128—Photo of boy when fourteen years old, with a healthy girl of ten for comparison



Fig. 370
Case 128—Left wrist showing rachitic changes in radius and ulna



Fig. 371
Case 128—Right knee showing rachitic changes in all three bones

CASE 129—RENAL OSTEO DYSTROPHY

(Figs 3 * and 3 3) R B male aged nine years. Admitted complaining of thirst Polyuria Walks badly Genu valgum Epiphyses enlarged Looks healthy but weight only forty three pounds. No history of renal disease in family but a brother born three years before patient died at five years with closely similar symptoms. Urine trace of albumin Urea concentration definitely abnormal Serum calcium 10·8 milligrams plasma phosphorus ·0 milligrams per 100 cubic centimetres. Blood urea 10 milligrams per 100 cubic centimetres. Radiographs showed rachitic changes with some woolliness. Diagnosed as renal rickets due to polycystic kidneys.



FIG 37*
Case 129—Wrists showing mixed rachitic and woolly changes in the radius and ulna The density of these tw bones is noteworthy

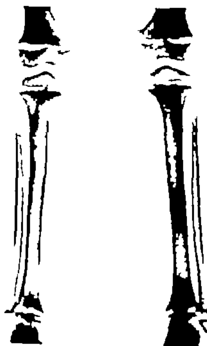


FIG. 373
Case 129—Legs showing rachitic changes t the epiphyseal discs

CASE 130—RENAL OSTEO-DYSTROPHY

(Figs. 374 to 376) H M., male aged fifteen years. Complained of pain in hips when walking for past four months worse towards end of day Complete relief on resting No obvious wasting Works in a warehouse No history of nephritis. Rolling gait. Thickening of wrists and ankles. Lies with legs abducted and rolled out Some limitation of all movements at hips except extension Urine large amount of albumin a few leucocytes and oxalate crystals. Urea concentration definitely subnormal. Chlorides markedly diminished. Blood urea within *normal limits 43 milligrams per 100 cubic centimetres. Plasma phosphorus above normal.* Radiographs showed rachitic changes at epiphyseal discs with some diminution in the density of the bones. Cyst in trochanteric region of left femur Treatment for six months resulted in considerable improvement confirmed by radiographic examination. There was no change in the cyst Free hip movements were regained.



Fig. 374

Case 130—Pelvis and hips showing widening of the femoral epiphyseal lines and slight displacement of the left femoral head on the neck Note the cyst in the left femur



Fig. 375

Case 130—Right wrist showing rachitic changes with a little erosion of the radial and ulnar metaphyses—early woolly changes Note the loss of definition of the cortex and medulla in both bones of the forearm



Fig. 376

Case 130—Wrist six months after Fig. 375, showing healing of the rachitic changes

CASE 131—RENAL OSTEO-DYSTROPHY

(Figs. 377 to 379.) S. B., male, aged five and a half years. Breast fed only partially. Weak on legs; did not walk till three and a half years, when some genu valgum was noticed. Deformity has gradually increased; now walks only with difficulty. Dark muddy complexion. Dwarfed. Height 33 inches (normal 41½ inches). Mentally backward. Epiphyses enlarged. Polyuria. Marked polydipsia. Urine: heavy cloud of albumin. Renal function very deficient. Radiographs showed marked changes at the epiphysial lines, with erosion of the adjacent cortices of some bones, and considerable general osteoporosis. Father is short and is said to have renal disease. About two years later the epiphysial enlargement had disappeared and a radiograph of a wrist showed almost normal epiphysial lines. The genu valgum had been gradually corrected. At the end of a further two years his improvement was maintained, though he was still well below the average in height and his urine showed a fair cloud of albumin.



Fig. 377
Case 131—Photo of child showing large head, narrow chest and deformed legs.



Fig. 378
Case 131—Wrist and knee on admission to hospital at five and a half years, showing osteoporosis of all the bones, and advanced rachitic changes at the epiphysial lines. Note the erosion of the cortex on the inner side of the lower end of the ulna.



Fig. 379
Case 131—Wrist and knee three and a half years after Fig. 378, showing the healing of the rachitic changes. Note there is still some juxta-epiphysial erosion of the cortices of the radius and ulna, and of the fibula.

CASE 132—RENAL OSTEO-DYSTROPHY

(Fig 380) A J male aged six years. Said to have been healthy till two and a half years old, when he developed genu valgum. Knees have become thickened. Walks only with difficulty Dwarfed. Height 35¼ inches (normal 43 *inches*) *Marked genu valgum Urine cloud* of albumin Urea concentration test shows deficiency Radiographs show no rachitic changes but some erosion of cortices of the metaphyses, with a slightly woolly appearance. In the lower ends of the femora the metaphyses show fractures with outward displacement of the epiphyses. (Reported by Dr Donald Paterson)



Fig. 380
Case 132—Knees showing the fractures in the metaphyses of both femora, with displacement outwards of the epiphyses.

CASE 133—RENAL OSTEO-DYSTROPHY with extensive fibrosis of the skeleton

(Figs. 381 to 385) M P male aged four years. Deformity of right leg noticed at birth. Feeble infant made slow progress. At ten months rickets was diagnosed. Treated by light, etc. Pale anaemic child. Head abnormally large. Chest barrel-shaped with Harrison's sulci. Slight rickety rosary Epiphyses enlarged Bowing of femora, and inward bowing of tibiae. Urine heavy cloud of albumin Blood urea 1 5 milligrams per 100 cubic centimetres. Calcium and phosphorus estimations not done owing to difficulty in *collecting sufficient blood. Radiographs showed typical woolly type of change at the wrists,* gross metaphyseal fragmentation with displacement of some epiphyses, *e.g.* elbows and hips, and cystic changes in the femora and tibiae Two weeks after admission child developed epistaxis, became drowsy with twitching of the limbs and within a fortnight he died in typical uraemic coma. Autopsy revealed atrophic and sclerotic kidneys. Right ureter greatly dilated right kidney only half the size of the left. No definite ureteral obstruction discovered. Pelvis and upper part of left ureter dilated there was a valve-like fold obstructing the entrance to the bladder Histologically there was much interstitial fibrosis of the kidney with obliteration of many glomeruli and hypertrophy of others. Tubules showed degenerative changes and much cystic dilatation. Section of a tibia showed trabeculae deficient both in number and in calcification, with some osteoid. Marrow showed much fibrous tissue In the skull and a rib atrophy of the marrow and replacement by fibrous tissue were found No parathyroid tumour or hypertrophy was discovered



Fig. 381
Case 133.—Arm showing woolly type of change in the radius and ulna at the wrist, and fragmentation of the metaphyses at the lower end of the humerus with displacement of the epiphyses



Fig 382

Case 133—Pelvis and hips showing indentation of the pelvis and gross osteoporosis of the femora with marked decalcification and deformity of the neck



Fig 384

Case 133—Microscopic section of tibia showing deficiency of cortex osteoclasts absorbing the bone and general fibrosis of the marrow

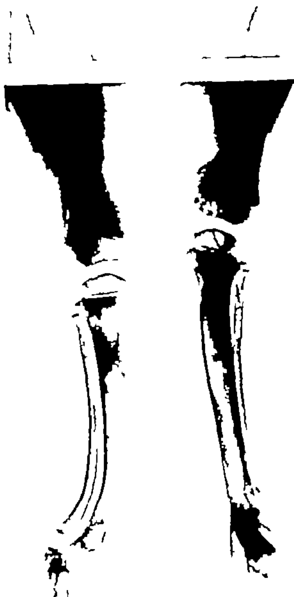


Fig 383

Case 133—Legs showing the deformity of the tibia and the cystic changes in the lower part of the femora and in the tibial shafts Decalcification of the cortices is seen in some places, notably on the inner side of the upper third of both tibiae There is a healed fracture of the left fibula The epiphyses are markedly porotic.



Fig 385

Case 133—Microscopic section of a osteo-chondral junction showing the [illegible] of cartilage columns very deficient bone formation and marked fibrosis

CHAPTER 23

RENAL OSTEO DYSTROPHY IN ADULTS

This is an uncommon condition in which skeletal changes chiefly of an osteoporotic type, occur in adults who have suffered from marked *renal insufficiency of long duration*. It corresponds in adults to what is usually called renal rickets in children and adolescents. Though it may begin in adult life in many cases the renal changes no doubt begin much earlier In 1937 Albright *et al* referred to three cases, one of which they reported in full, of what they called Renal Osteitis Fibrosa Cystica, a condition with the following features *marked renal insufficiency of long duration* phosphorus retention with high plasma phosphorus slight reduction in the serum calcium marked acidosis calcium deposits in the neighbourhood of joints including those of the fingers *extreme calcification of the media of arteries* generalised osteitis fibrosa of the bones and enormous enlargement of all the parathyroids. The parathyroid hyperplasia is regarded as secondary to the renal insufficiency There is no doubt however that neither enlargement of the parathyroids nor osteitis fibrosa of the skeleton is necessarily present, and that generalised osteoporosis, *with or without some fibrosis, is the essential change in the skeleton.* Cottrell (1947) maintains that cases without parathyroid enlargement are exceptional, yet in a small series of seven published and unpublished cases we have studied no enlargement of the glands was discovered post mortem in three of them definite enlargement was found in three while the remaining case is still alive and the condition of the parathyroids is unknown. This affection is certainly uncommon, particularly if one excludes the adults in whom the disease is known to have begun in adolescence. Cottrell found few cases over the age of thirty but two of the oldest *were fifty-five and sixty respectively while his own case was a woman who died of uraemia* at seventy five years, and was regarded by him as Renal Osteitis Fibrosa superimposed on senile osteoporosis. Section of the bones in this case revealed " marked atrophy with slight, but definite osteitis fibrosa, yet no evidence of hyperplasia of the parathyroids was discovered at autopsy Radiographs in addition to the general osteoporosis showed pseudo-cystic areas in several bones, and discrete patches of rarefaction in the skull. *The radiographic changes* in the skull in these cases are somewhat coarser than in hyperparathyroidism according to Brailsford (1948) who also reports multiple incomplete fractures. We know of two cases who developed multiple spontaneous fractures both cases died of uraemia in neither case was any hyperplasia of the parathyroids discovered at autopsy In another renal case a man of twenty-eight there was subperiosteal new bone formation on several of the porotic long bones in addition to calcification of arteries and other soft tissues. Snapper (1949) and some *others regard the renal acidosis as probably responsible for the osteitis fibrosa.* Marked hypercalcaemia is in favour of primary parathyroid hyperplasia, whereas when the renal changes are primary and the parathyroid enlargement secondary the serum calcium is much more likely to be low or at most only slightly elevated. In the case fully reported by Albright *et al* (1937) a man of forty-five years with a painful swelling of a hand for two months, there was metastatic calcification of the fingers and the region of *both elbows and both* acromio-clavicular joints. Biopsy of a tibia showed rapid de-ossification by osteoclasts, *new bone formation by a few osteoblasts* with normal calcification of osteoid, and definite fibrosis of the marrow In this case all four parathyroids were enlarged. In a woman of twenty-three years with a history of weakness for only ten months Magnus and Scott (1936) found at autopsy that the skull cap though of normal thickness could be bent with ease in this case three of the parathyroids were enlarged but there was no fibrosis of the bones As in younger patients *with renal osteo-dystrophy when the parathyroids are enlarged* it is the chief cells which proliferate especially with some increase in the oxyphil cells occasionally

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CASE 134—RENAL OSTEO-DYSTROPHY in an adult

(Figs. 386 to 389.) F. S. male aged twenty five years at time of death (June 194) Said to have had rickets in childhood. In 1940 when aged twenty years supracondylar osteotomy of left femur performed for genu valgum which had been gradually increasing In January 1944 complained of pain in right leg In September 1944 following recent complaint of pain in left thigh the femur suddenly snapped while he was walking Radiographs revealed two fractures in left femur the lower being the osteotomy imperfectly united Urine 2 300 cubic centimetres per diem Albumin present Urea concentration lowered Blood urea varied from 33 to 280 *milligrams per 100 cubic centimetres during following nine months* Blood count showed nothing special. White cells 9,600 Serum calcium estimations at various dates gave figures of 4·4 to 9·0 milligrams per 100 cubic centimetres and plasma phosphorus 2·2 to 6·2 milligrams per 100 cubic centimetres Alkaline phosphatase raised E.S.R. raised Pyuria associated with enterococcus developed three days before his death from uraemia. Mild tetanic spasm preceded coma. *Post mortem* dilatation of ureters pelvis and calices. Chronic nephritic changes in kidneys. Careful search revealed no enlarged parathyroids Pituitary normal. Section of the fractures showed a large proportion of cartilage in the callus Radiographs at various dates showed general osteoporosis "cysts" in both femora and the left tibia, and complete or incomplete fractures in right femur left femur (two) left tibia and right and left ulnae (healed) Vault of skull thin Vertebral bodies biconcave (Under Mr H H Langston.)



Fig 386
Case 134—Lateral view of spine showing osteoporosis, biconcave vertebral bodies and biconvex discs.

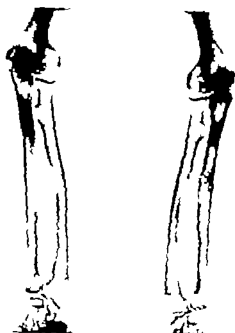


FIG. 337

Case 134—Arms showing osteoporosis and healed fractures in shafts of both ulna



FIG. 388 FIG. 389

Case 134. Figure 388—Femora showing osteoporosis with poorly developed cortices, a cyst in each femur, an incomplete pseudo-fracture in the subtrochanteric region of the right and two imperfectly united fractures in the left. Figure 389—Legs showing osteoporosis, a fracture in the right tibia (lateral view suggests this is incomplete) and at least one small cyst in left tibia. The osteoporosis is more marked in the left leg, presumably due to the immobilisation required for the fractured left femur.

CASE 135—RENAL OSTEO-DYSTROPHY in an adult

(Figs. 390 to 393.) D. W. male aged twenty-eight years (1040). Frequency of micturition for years. Admitted to hospital for nephritis in 1030. Served six years in Army being classed A1 throughout. After a bad cold feet became painful twelve months ago. For the past four months has complained of weakness of legs, lassitude and shortness of breath. Sallow muddy complexion ? slightly jaundiced. Square squat head flat on top. Parotids visible. Breath smells of urea. Clubbing of fingers. Prominent sterno-clavicular joints. Rickety rosary. Kyphosis. Urine low specific gravity. Albumin present. Blood examination urea 193 milligrams, serum calcium 11.1 milligrams, plasma phosphorus 10 milligrams per 100 cubic centimetres. Alkaline phosphatase 31.5 units. Radiographs showed marked generalised osteoporosis with fluffiness of cortices of some long bones and subperiosteal new bone formation on others, including both femora. Definite erosion of the cortices of several of the metacarpals and phalanges. Calcification seen in the arteries and in the periarticular tissues of the elbows, wrists and symphysis pubis and in the finger tips. Outer table of skull partially decalcified and woolly. (Under Dr P. H. O'Donovan and Mr F. Crooks.)



FIG. 390

Case 135—Skull showing woolly appearance of outer table. Print gives false impression of the density of the bones.



FIG. 391

Case 135—Left hand showing erosion of the cortices of many of the bones, particularly of the terminal phalanges, and metastatic calcification to the inner side of the wrist joint and in the tips of the digits. Note the calcification of arteries in one interdigital space and the fracture of one phalanx.

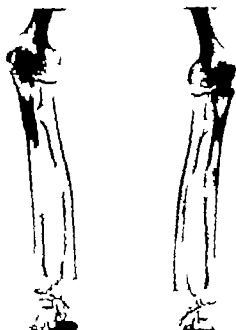


Fig. 387

Case 134—Arms showing osteoporosis and healed fractures in shafts of both ulnae.



Fig. 388

Fig. 389

Case 134 Figure 388—Femora showing osteoporosis with poorly developed cortices, yet in each femur an incomplete pseudo-fracture in the subtrochanteric region of the right and two imperfectly united fractures in the left. Figure 389—Legs showing osteoporosis, a fracture in the right tibia (lateral view suggests this is incomplete) and at least one small cyst in left tibia. The osteoporosis is more marked in the left leg, presumably due to the immobilisation required for the fractured left femur.

CASE 135—RENAL OSTEO-DYSTROPHY in an adult

(Figs. 390 to 393.) D. W., male aged twenty-eight years (1940). Frequency of micturition for years. Admitted to hospital for nephritis in 1930. Served six years in Army, being classed A1 throughout. After a bad cold feet became painful twelve months ago. For the past four months has complained of weakness of legs, lassitude and shortness of breath. Sallow, muddy complexion ? slightly jaundiced. Square, squat head flat on top. Parotids visible. Breath smells of urea. Clubbing of fingers. Prominent sterno-clavicular joints. Rickety rosary. Kyphosis. Urine low specific gravity. Albumin present. Blood examination: urea 103 milligrams, serum calcium 11.1 milligrams, plasma phosphorus 10 milligrams per 100 cubic centimetres. Alkaline phosphatase 31.5 units. Radiographs showed marked generalised osteoporosis with fluffiness of cortices of some long bones and subperiosteal new bone formation on others, including both femora. Definite erosion of the cortices of several of the metacarpals and phalanges. Calcification seen in the arteries and in the periarticular tissues of the elbows, wrists and symphysis pubis, and in the finger tips. Outer table of skull partially decalcified and woolly. (Under Dr P. H. O'Donovan and Mr F. Crooks.)



FIG. 390

Case 135—Skull showing woolly appearance of outer table. Print gives false impression of the density of the bones.



FIG. 391

Case 135—Left hand showing erosion of the cortices of many of the bones, particularly of the terminal phalanges, and metastatic calcification to the inner side of the wrist joint and in the tips of the digits. Note the calcification of arteries in one interdigital space and the fracture of one phalanx.



Fig. 382

Case 135—Pelvis showing osteoporosis and metastatic calcification in the *region of the symphysis pubis.*



Fig 383

Case 135—Legs showing osteoporosis with fluffy appearance of the cortices and subperiosteal hyperostosis in certain places on the tibia *(Print is unduly dense.)*

CHAPTER 34

FANCONI'S SYNDROME

In 1933 de Toni published a paper on "the relations between renal rickets and renal diabetes" and he refers to a case of renal diabetes published in 1931 by Fanconi in which apparently there was retardation of growth. In 1936 Fanconi published an article on Renal Glycosuria with Hypophosphataemic Rickets. By some de Toni's name is linked with Fanconi's in the title of this syndrome. In 1943 McCune *et al.* published a case, a boy of nine years with multiple fractures, and they reviewed twenty-eight other cases. They refer to the case of a child of three years, with marked rachitic changes and albumin and sugar in the urine, published by Lignac in 1924.

The features of the syndrome are resistant and intractable rickets, hypophosphataemia, renal glycosuria, acidosis, in some cases cystinosis and in some calcinosis.

Though frequently not discovered till later the condition usually begins within the first two years of life, but there were two adults in the series reviewed by McCune *et al.* Hunter (1935) published a case, a male of thirty-five, in whom the onset of general osteoporosis with renal glycosuria occurred in the thirty-first year. The neck was explored but no parathyroid tumour was found.

Early signs are retarded development, loss of appetite, gastro-intestinal disturbance, bouts of fever, and albumin and casts in the urine. Apparently albuminuria is not invariably present. The serum calcium is normal, the plasma phosphorus is low, the plasma phosphatase is raised. The excretion of calcium and phosphorus is excessive. The spleen and liver are sometimes enlarged. The outlook is unfavourable, but the condition is not invariably fatal. Rachitic bowing of the bones and fractures may occur. McCune *et al.* found seven cases of rickets combined with cystinuria. They do not regard the Fanconi syndrome as a sharply defined clinical entity—it merges into hypophosphataemic renal rickets on the one hand and "poorly understood cystine rickets" on the other. Fanconi suggested the condition is tubular renal rickets as opposed to glomerular renal rickets, and results from hereditary inadequacy of the tubular epithelium. The osteoporosis is marked, and in those beyond the age for rickets it is the only skeletal change. In 1926 we briefly referred to two cases, aged six and eleven years respectively, with what appeared to be typical renal rickets, and in whose urine sugar as well as albumin was found. The first case showed enlargement of the liver and spleen and by her eighth year she was a typical renal dwarf. She died about a year later. In the other case, with marked osteoporosis and rickety changes, the glycosuria was proved to be renal in origin. (See Cases 136 and 137.)

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CASE 136—FANCONI'S SYNDROME

(Figs. 394 and 395.) M. W., girl, aged eleven years. Had severe attack of measles in first year and whooping cough and pneumonia at three years. Always been delicate and undersized. Two years ago complained of stiffness of knees; deformity of left knee noticed a year ago. Enlargement of wrists during past three months. Alert and bright child but backward at school. No undue thirst or frequency of micturition. Height just under 4 feet (normal 53 inches). Enlargement of epiphyses at knee and wrists. Genu valgum 4½ inches. No obvious beading of ribs. Urine: average daily output 26 to 30 ounces. Albumin and sugar present. Few oxalate crystals and an occasional cast. The glycosuria was proved to be renal. Radiographs showed some general hypocalcification of the skeleton and advanced rachitic changes at the epiphysial lines. Five years later when admitted for fracture of a femur radiographs of a wrist still showed the bones poorly calcified but the rachitic changes had almost disappeared, though the epiphyses were still markedly enlarged.



Fig. 394

Case 136—Wrist showing poorly calcified bones and marked rachitic changes in the radius and ulna.

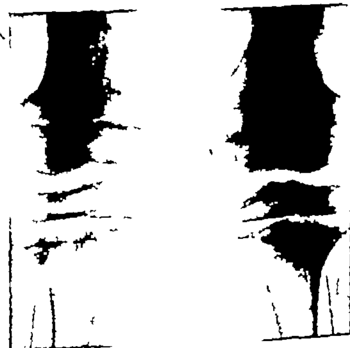


Fig. 395

Case 136—Knees showing unduly translucent bones and advanced rachitic changes at all epiphyseal lines.

CASE 137—FANCONI'S SYNDROME

(Figs. 396 and 397) I. P. girl aged six years (1931). All well till two years ago when had measles followed by whooping cough. Since then knock knee developed and she has failed to put on weight to a normal extent. A year ago seen by Dr G. F. Still who found epiphyses enlarged and also enlargement of liver and spleen. Has grown in height but not in weight which is only 27½ lb (normal 53 lb.). Stomatitis eighteen months ago. Laryngitis last year. Has not walked for over a year. Appetite very poor. Abdomen large. Liver and spleen enlarged but said to be smaller than a year ago. Glands in neck. Genu valgum. Coxa vara. All epiphyses large. *Beading of ribs. Some contracture of hips. Urine: clouds of albumin*; sugar also present. With treatment began to gain weight and liver and spleen became smaller but in two months was losing weight again. Two years later could not even sit for long as soon got tired. Arms then showed juxta-epiphysial angulation at upper ends of the humeri and lower ends of both radii. The lower ends of the radii were freely mobile on the shafts. Marked flexion deformity in the lower thirds of the femora with limitation of movement. Marked scoliosis present. Pigeon breast with bilateral groove in the line of the costo-chondral junctions. ? fractures of ribs present. Spleen still slightly enlarged. Lymph glands palpable all over body. All epiphyses large. Radiographs showed gross osteoporosis, with deformities associated with fractures and displacement of epiphyses. Regarded as definite renal dwarf. Died of uraemia about a year later (1934) aged nine years.



FIG. 396

Case 137.—Legs showing extreme osteoporosis and deformities in the femora, apparently due to collapse of the metaphysis in one and bending and partial fracture of the lower third of the shaft in the other.

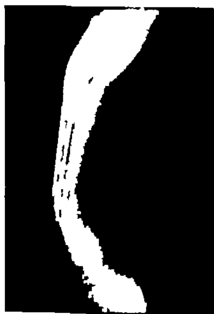


FIG. 397

Case 137.—Forearm showing deformity at both ends of the radius and ulna due to fractures and at the lower ends, to displacement of epiphyses in addition.

CASE 136—FANCONI'S SYNDROME

(Figs. 394 and 395.) M. W., girl, aged eleven years. Had severe attack of measles in first year and whooping cough and pneumonia at three years. Always been delicate and undersized. Two years ago complained of stiffness of knees; deformity of left knee noticed a year ago. Enlargement of wrists during past three months. Alert and bright child but backward at school. No undue thirst or frequency of micturition. Height just under 4 feet (normal 53 inches). *Enlargement of epiphyses at knee and wrists. Genu valgum 4½ inches. No obvious* beading of ribs. Urine: average daily output 26 to 30 ounces. Albumin and sugar present. Few oxalate crystals and an occasional cast. The glycosuria was proved to be renal. Radiographs showed some general hypocalcification of the skeleton and advanced rachitic changes at the epiphysial lines. Five years later when admitted for fracture of a femur radiographs of a wrist still showed the bones poorly calcified but the rachitic changes had almost disappeared, though the epiphyses were still markedly enlarged.



Fig. 394
Case 136—Wrist showing poorly calcified bones and marked rachitic changes in the radius and ulna.

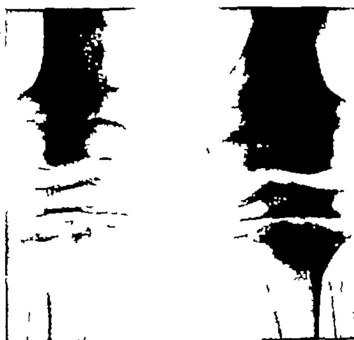


Fig. 395
Case 136—Knees showing [illegible] translucent bones and advanced rachitic changes at all epiphyseal lines.

CASE 137—FANCONI'S SYNDROME

(Figs. 396 and 397.) I. I. girl aged six years (1921). All well till two years ago when had measles followed by whooping cough. Since then knock knee developed and she has failed to put on weight to a normal extent. A year ago seen by Dr G. F. Still who found epiphyses enlarged and also enlargement of liver and spleen. Has grown in height but not in weight which is only 27½ lb (normal 43 lb). Stomatitis eighteen months ago. Laryngitis last year. Has not walked for over a year. Appetite very poor. Abdomen large. Liver and spleen enlarged but said to be smaller than a year ago. Glands in neck. Genu valgum. Coxa vara. All epiphyses large. Beading of ribs. Some contracture of hips. Urine clouds of albumin, sugar also present. With treatment began to gain weight and liver and spleen became smaller but in two months was losing weight again. Two years later could not even sit for long as soon got tired. Arms then showed juxta-epiphysial angulation at upper ends of the humeri and lower ends of both radii. The lower ends of the radii were freely mobile on the shafts. Marked flexion deformity in the lower thirds of the femora with limitation of movement. Marked scoliosis present. Pigeon breast with bilateral groove in the line of the costo-chondral junctions. ? fractures of ribs present. Spleen still slightly enlarged. Lymph glands palpable all over body. All epiphyses large. Radiographs showed gross osteoporosis with deformities associated with fractures and displacement of epiphyses. Regarded as definite renal dwarf. Died of uraemia about a year later (1924) aged nine years.



Fig. 396

Case 137.—Legs showing extreme osteoporosis and deformities in the femora apparently due to collapse of the metaphysis in one and bending and partial fracture of the lower third of the shaft in the other.

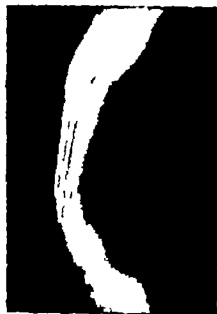


Fig. 397

Case 137.—Forearm showing deformity at both ends of the radius and ulna due to fractures and at the lower ends, to displacement of epiphyses in addition.

: 136—FANCONI'S SYNDROME

. 394 and 395) M W girl aged eleven years. Had severe attack of measles in first year
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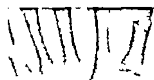
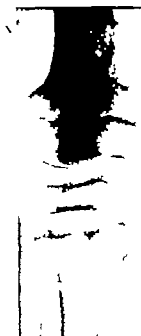




FIG. 394
Case 136—Wrist showing poorly calcified bones nd marked rachitic changes in the radius and ulna.





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CASE 137—FANCONI'S SYNDROME

(Figs 396 and 397) [illegible] girl aged six years (1921) All well till two years ago when had measles followed by whooping cough Since then knock knee developed and she has failed to put on weight to a normal extent A year ago seen by Dr C F Still who found epiphyses enlarged and also enlargement of liver and spleen Has grown in height but not in weight which is only 27½ lb (normal [illegible] lb) Stomatitis eighteen months ago Laryngitis last year Has not walked for over a year Appetite very poor Abdomen large Liver and spleen enlarged but said to be smaller than a year ago Glands in neck Genu valgum Coxa vara All epiphyses large Beading of ribs Some contracture of hips Urine clouds of albumin sugar also present With treatment began to gain weight and liver and spleen became smaller but in two months was losing weight again Two years later could not even sit for long as soon got tired Arms then showed juxta-epiphysial angulation at upper ends of the humeri and lower ends of both radii The lower ends of the radii were freely mobile on the shafts Marked flexion deformity in the lower thirds of the femora with limitation of movement Marked scoliosis present Pigeon breast with bilateral groove in the line of the costo-chondral junctions [illegible] fractures of ribs present Spleen still slightly enlarged Lymph glands palpable all over body All epiphyses large Radiographs showed gross osteoporosis with deformities associated with fractures and displacement of epiphyses. Regarded as definite renal dwarf Died of uraemia about a year later (1924) aged nine years.



Fig. 396

Case 137 —Legs showing extreme osteoporosis and *deformities in the femora apparently due to collapse* of the metaphysis in one and bending and partial fracture of the lower third of the shaft in the other

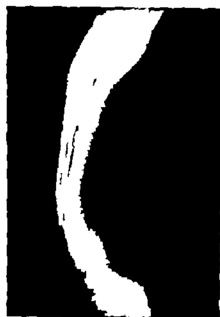


Fig. 397

Case 137—Forearm showing deformity at both ends of the radius and ulna due to *fractures* and at the lower ends, to displacement of epiphyses in addition

CASE 136—FANCONI'S SYNDROME

(Figs. 394 and 395.) M. W., girl aged eleven years. Had severe attack of measles in first year and whooping cough and pneumonia at three years. Always been delicate and undersized. Two years ago complained of stiffness of knees; deformity of left knee noticed a year ago. Enlargement of wrists during past three months. Alert and bright child but backward at school. No undue thirst or frequency of micturition. Height just under 4 feet (normal 53 inches). Enlargement of epiphyses at knee and wrists. Genu valgum 4½ inches. No obvious beading of ribs. Urine: average daily output 20 to 30 ounces. Albumin and sugar present. Few oxalate crystals and an occasional cast. The glycosuria was proved to be renal. Radiographs showed some general hypocalcification of the skeleton and advanced rachitic changes at the epiphysial lines. Five years later when admitted for fracture of a femur radiographs of a wrist still showed the bones poorly calcified but the rachitic changes had almost disappeared, though the epiphyses were still markedly enlarged.



Fig. 394
Case 136—Wrist showing poorly calcified bones and marked rachitic changes in the radius and ulna.

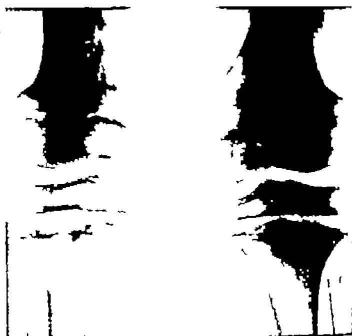


Fig. 395
Case 136—Knees showing [illegible] trabeculae of bone and advanced rachitic changes at all epiphysial lines.

CASE 137—FANCONI'S SYNDROME

(Figs. 396 and 397.) *F. J., girl, aged six years (1931). All well till two years ago, when had* measles followed by whooping cough. Since then knock knee developed and she has failed to put on weight to a normal extent. A year ago seen by Dr. C. F. Still, who found epiphyses enlarged and also enlargement of liver and spleen. Has grown in height but not in weight, which is only 27¼ lb. (normal 45 lb.). Stomatitis eighteen months ago. Laryngitis last year. *Has not walked for over a year. Appetite very poor. Abdomen large. Liver and spleen* enlarged, but said to be smaller than a year ago. Glands in neck. Genu valgum. Coxa vara. All epiphyses large. Beading of ribs. Some contracture of hips. Urine: clouds of albumin; sugar also present. With treatment began to gain weight and liver and spleen became smaller, but in two months was losing weight again. Two years later could not even sit for long, as *soon got tired. Arms then showed juxta-epiphysial angulation at upper ends of the humeri* and lower ends of both radii. The lower ends of the radii were freely mobile on the shafts. Marked flexion deformity in the lower thirds of the femora with limitation of movement. Marked scoliosis present. Pigeon breast with bilateral groove in the line of the costo-chondral junctions. ? fractures of ribs present. Spleen still slightly enlarged. Lymph glands palpable *all over body. All epiphyses large. Radiographs showed gross osteoporosis with deformities* associated with fractures and displacement of epiphyses. Regarded as definite renal dwarf. Died of uraemia about a year later (1934) aged nine years.



Fig. 396

Case 137.—Legs showing extreme osteoporosis and deformities of the femora, apparently due to collapse of the metaphysis in one, and bending and partial fracture of the lower third of the shaft in the other.

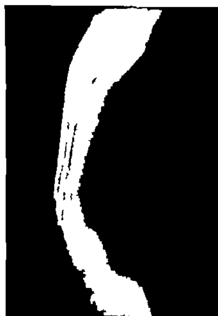


Fig. 397

Case 137.—Forearm showing deformity at both ends of the radius and ulna due to fractures and, at the lower ends, to displacement of epiphyses in addition.

CHAPTER 25

SENILE OSTEOPOROSIS

In this condition which affects elderly people osteoporosis of the spine is the chief feature. The skeletal changes are definitely not those of osteomalacia. Good reviews of this subject have been published by Black *et al* (1941) and Burrows and Graham (1945)

Hereditary and familial influences play no part in the incidence.

Sex—Females are more than twice as frequently affected as are males.

Age—Burrows and Graham found it occurred most commonly in people from the fifty-fifth to the sixty-fifth year Black *et al* in their series of 208 cases aged from forty five to eighty-seven years found the average age was sixty two

Etiology—The cause is not known with certainty The fact that elderly females are the chief sufferers suggests diminishing physical activity may play an important part in the causation Owing to the absence of normal mechanical stimuli bone formation lags behind bone absorption (Baker 1939) The degree of porosis is aggravated if the patient is confined to bed for any reason *e.g* for the treatment of a fracture of the neck of the femur The suggestion is made by Lyon (1937) that it is due to increase in the basophil cells of the anterior pituitary since the generative glands are in a state of involution

Signs and symptoms—Most cases are thin and only rarely are they fat There may be no symptoms the condition being found by chance. The usual complaint is one of pain in the lower dorsal and lumbar regions, sudden in onset and perhaps accompanied by a distinct sensation of a snap or crack in the back when the collapse of a vertebral body occurs. This crushing of a body may be caused by any exceptional effort such as lifting a weight or coughing As a rule the damage occurs when the spine is flexed, but Burrows and Graham (1945) found it occurred quite often with the spine in extension. The pain may be acute at first but soon diminishes and becomes chronic varying in degree with the amount of exercise. Only exceptionally does the pain radiate Sensory changes in the legs may occur but are very seldom present There is kyphosis sometimes with a small element of scoliosis and one spinous process is slightly prominent and tender Some limitation of movement is common. Achlorhydria was present in a third of the cases collected by Burrows and Graham.

Blood Examination reveals nothing significant. A negative calcium balance is said to be usually present

Radiographic appearances—There is osteoporosis of the spine diminishing in severity from below upwards. The vertebral bodies become slightly biconcave and the discs biconvex conspicuously so in the lower dorsal and lumbar regions. One two or even more of the bodies show signs of crushing or collapse The collapse or wedging affects the upper surface towards the front only occasionally towards one side there may be some increased density and forward projection of the crushed surface The body most frequently crushed is the first lumbar and the next in frequency are the two bodies above and the two below this vertebra. Only occasionally does a body higher than the eleventh dorsal show collapse. Sometimes the upper surface of a body is deeply hollowed without signs of crushing of the anterior surface or the whole body may be considerably reduced in thickness without obvious signs of fracture Osteoarthritic lipping and narrowing of the discs may be present but these are usually seen somewhat higher in the mid-dorsal region and they may be accompanied by some general wedging of the bodies all being the result of the dorsal kyphosis of long standing The remainder of the skeleton also shows osteoporosis but not to the degree seen in the spine The pelvis is not distorted

Prognosis—Under suitable treatment the symptoms disappear and, provided nothing occurs to cause further vertebral collapse, the patient may remain reasonably free from pain for some years. The osteoporosis remains unchanged.

Complications—Fracture of a long bone may occur from comparatively slight force, but the spine is the only site of multiple fractures. Pseudo-fractures of the Looser type have not been reported. Renal calculi may occur.

Pathology—There is extreme osteoporosis of the vertebral bodies but the changes differ from those seen in osteomalacia in the absence of osteoid. If osteoid is present at all, the seams are only of normal thickness (Burrows and Graham 194). All the trabeculae and the cortex are thinned, and the vascular canals widened, with negligible lacunar absorption (Jaffe 1933). The bone is good enough but there is too little of it. There is no fibrosis except in the proximity of collapse of the spongy bone or a definite fracture.

Diagnosis—The most frequent difficulty that arises is in the exclusion of metastatic carcinomatous deposits as responsible for part of the radiographic changes, particularly for collapse of a body. Hyperparathyroidism occasionally arises as an alternative diagnosis; the degree of decalcification of the whole skeleton and the raised serum calcium should give rise to doubts as to senile osteoporosis being responsible. In osteomalacia the osteoporosis is generalised and not specially severe in the spine, blood examination reveals low phosphorus and high phosphatase figures, while many of the cases are young women.

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CASE 138—SENILE OSTEOPOROSIS

(Fig 398) Mrs M., aged sixty five years (January 1930) Six months ago was operated upon for carcinoma of colon. Satisfactory excision accomplished. Six weeks ago sudden pain in lower back no recent injury Pain caused by any movement such as turning in bed, but not by walking Is better when up and about. Pain does not radiate Dorso-lumbar kyphosis present with two spinous processes ? eleventh and twelfth dorsal, prominent broad and tender Movements of spine limited, but not markedly No paralysis. Reflexes exaggerated. Radiographs of spine taken before the abdominal operation showed osteoporosis only films taken since the onset of pain showed, in addition to marked osteoporosis, crushing of D 12 and L 4 bodies, and reduction in depth of other vertebral bodies. No convincing signs of metastases. A period of recumbency in a plaster shell followed by the use of a leather corset resulted in complete relief though radiographs showed some further collapse of vertebral bodies. Two years later was able to row and do much heavy housework. Serum calcium then 10·3 milligrams and plasma phosphorus 4 1 milligrams per 100 cubic centimetres Ten years later was still in surprisingly good health (Under Mr Harold Edwards.)

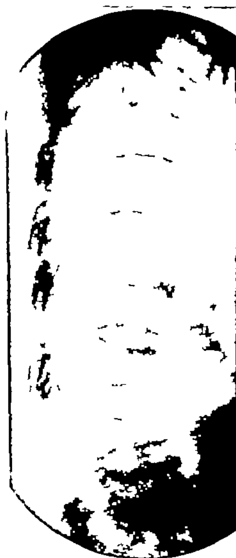


Fig 398

Case 138—Lateral view of lower dorsal spine showing osteoporosis, biconcave bodies many of which are reduced in depth biconvex discs, and a crush fracture of D 12, and possibly also of D 6 Some early lipping of a few bodies

CASE 139 SENILE OSTEOPOROSIS

(Figs. 399 to 401.) Mrs. S., aged fifty-six years. Pain in back for two months. Injury of back eight years previously, none since. Only mild kyphosis. Lumbar region rigid. Plantar reflexes not obtained. Urine: bacillus coli infection. Blood serum calcium 9·4 milligrams, plasma phosphorus 2·8 milligrams per 100 cubic centimetres. Alkaline phosphatase 6 (normal). Treated in plaster bed. Radiographs showed osteoporosis with some collapse of D 11 and L 1 and 3 and complete collapse of D 9. No definite signs of metastases. Five months later felt something give in her back while she was drying herself after a bath. Complains of lumbar pain. No abrupt kyphosis. Movement of lumbar spine limited. Radiographs of spine showed L 4 partially collapsed. Spinal brace ordered. Six months later again complained that "something went" in her back. Radiographs showed some increase of collapse of D 11 body. Ten months later back rather surprisingly flat. Aches at times in region of D 11. Still wearing brace but anxious to discard it. Radiographs show no change. All doubts as to the possibility of the presence of metastases can now be discarded.



Fig. 399

Case 139—Antero-posterior view of spine showing the intense osteoporosis. Signs of collapse in L 1, 3 and 4.



Fig 400
Case 139—Lateral view of spine showing osteoporosis, hollowing out of upper surface of D 11 L 1 L 3 and L 4 bodies, with some irregularity in density and biconvex discs.



Fig 401
Case 139—Lateral iew of spine showing the complet ollapse f D 9 body

LIPOID GRANULOMATOSIS

Reticulo-endotheliosis   Lipoidoses   Xanthomatosis

This is a group of conditions which have gradually come to be regarded as related on account of the fundamental pathology common to them all. Only in some is there an actual deposit of a lipoid in the pathological lesion, the lipoid varying with the particular clinical condition. In four of the five members of the group osseous lesions occur.

Eosinophilic granuloma is the name suggested by Jaffe and Lichtenstein (1940) and now used to an increasing extent to denote a clear lesion in a bone which contains inflammatory granulomatous material and shows histologically proliferation of histiocytes and eosinophils but no deposit of lipoid. In some cases of this condition the lesions are multiple and the radiographic appearances closely resemble those seen in Hand-Schüller-Christian disease, in which the special histological features are the presence of foam cells containing cholesterol esters and an absence of excess of eosinophils. *Though not the first to suggest that eosinophilic granulomata were allied to the lipoidoses*, Jaffe and Lichtenstein in 1944 expressed the opinion that it was "logically probable" that lesions in Hand-Schüller-Christian disease originally resemble eosinophilic granulomas, the cells having submitted later to collagenisation and lipoidisation.

Though radiologically these two conditions may be very similar, cases of eosinophilic granuloma lack the clinical syndrome characteristic of Hand-Schüller-Christian disease. Allied to these two conditions is Letterer-Siwe disease, to give it one of its many names, a disease in which again there is proliferation of reticular cells and histiocytes but without the secondary precipitation of cholesterol. This is an acute and usually fatal disease which affects infants and in most cases there are destructive bone lesions similar to those seen in Hand-Schüller-Christian disease; only exceptionally is the disease chronic and then apparently it becomes Hand-Schüller-Christian disease.

Another allied condition is Niemann-Pick disease, almost exclusively met with in Jewish female children and in which lipoid histiocytosis is of the phosphatide type—a cholesterol phosphatide mixture. In this condition, though yellowish deposits have been found in the bone marrow post mortem, no changes in the skeleton are demonstrable by X-rays, so it will not be further considered.

There appears to be strong evidence in favour of regarding the lesions in Hand-Schüller-Christian disease as an *inflammatory response to an unknown infection, the lipoidisation* occurring secondarily, and not the result of a primary error of metabolism. On the other hand, in Gaucher's disease an error of metabolism does appear to be responsible for the [lip]oidosis. In this condition the lipoid deposited is a cerebroside, kerasin. Though the gross [en]largement of the spleen, and to a less extent of the liver, rather dominates the clinical [pic]ture in Gaucher's disease, bone changes are common, so the disease calls for our [con]sideration.

Useful discussions of the whole subject have been published by Jaffe and Lichtenstein [(19]44) and Snapper (1949).

Finally, opinion is increasingly inclined towards placing among the lipoidoses the form [of] chondro-osteo-dystrophy known as Gargoylism. It may also be recalled that a few but [on]ly a few foam cells may be found at sites of degeneration in the fibrotic lesions of undoubted [ca]ses of polyostotic fibrous dysplasia.

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CASE 140—EOSINOPHILIC GRANULOMA

(Figs. 402 and 403.) V G male aged two and a half years. Began to walk at fourteen months. Limping for past four months. Fairly healthy boy. Slight irritability of left hip. Radiographs showed large cystic lesion in left ilium. Deficiency with hard well-defined edge felt in left fronto-parietal region of skull confirmed by radiograph. Low-grade pyrexia. E.S.R. 38 (Westergren). Haemoglobin 05 per cent. Differential and total white count normal. Mantoux and patch tests negative. Sternal puncture revealed no gross abnormality. Blood cholesterol 1/8 milligrams per cent. All further radiographs including that of the chest were negative. Biopsy of iliac tumour performed. Dr H. A. Sissons reported: Histological structure is characteristic of eosinophilic granuloma. Some vacuolated cells are present and may be lipoid-containing cells of the type seen in the lesions of Hand Schuller-Christian's Syndrome. This appears to be a case of eosinophilic granuloma near the border line between this condition and the Hand Schüller Christian disease. (Under Mr C. M. Squire.)



Fig. 402

Case 140—Pelvis showing the large eosinophilic granuloma in the left ilium.

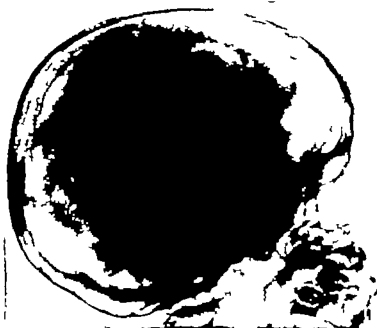


Fig. 403

Case 140. Skull showing the appearance produced by the granulomas, which is indistinguishable from that seen in typical case of Hand-Schüller Christian disease. Note the base and the sella are unaffected.

CHAPTER 38

HAND SCHULLER CHRISTIAN DISEASE

In this uncommon condition there is characteristically a localisation of a lipoid granuloma of bone (Moreau 1930). It is characterised by multiple defects in the skull and other bones, exophthalmos and diabetes insipidus with or without other signs of pituitary dysfunction such as dwarfism and infantilism and even occasionally dystrophia adiposa genitalis. In 1893 Hand found yellow deposits in the calvaria of a case with polyuria and thought they were due to tuberculosis. In 1915 Schuller reported two cases and suggested involvement of the pituitary was responsible for the diabetes insipidus. In 1920 Christian described a typical case and in 1928 the characteristic foam cells containing cholesterol esters were described by Rowland. Since that date many cases have been reported. Useful reviews have been published by Moreau (1930) and Snapper (1949). In 1930 Chester pointed out that the lesions were primarily granulomata and that the deposit of cholesterol was secondary.

Hereditary and familial influences play no part in the incidence. Only one instance of two sisters being affected has been reported.

Sex—Both sexes are affected, males rather more commonly.

Age—It occurs typically in early childhood from the first to the tenth year but occasionally in adolescents or adults. The oldest sufferer reported was over fifty years of age.

Etiology—The actual cause is unknown. There appears to be wide support for the idea that the primary fault is in the bones where possibly as a result of an unknown infection granulomata are formed, the foam cells being the result of secondary deposits of cholesterol and cholesterol esters in histiocytes, and that there is no primary disturbance of cholesterol metabolism. In most cases there is no striking increase of the cholesterol in the blood as there is in tuberous xanthoma of the skin; the two conditions are not really related.

Distribution of the lesions. In the great majority of cases the skull is affected and in those with the typical syndrome the base is involved with invasion of the pituitary and also of the orbits. Quite exceptionally the skull is clear of lesions when other bones are affected. The bones most commonly showing lesions apart from the skull are the spine, ilium, mandible and the long bones, particularly the femora. Less commonly the ribs, humeri, tibiae and sternum are affected. Lesions in the skin are not uncommon and they may be found also in the following soft tissues: the liver (accompanied by jaundice), the spleen, pelvis of the kidney, mesentery, brain, lungs, larger blood vessels and lymphatic glands. The hands and feet appear to escape as a rule but a metacarpal head and some phalanges were affected in an adult male in whom the presence of foam cells was proved though the typical syndrome of Hand-Schuller-Christian disease was absent (Ponseti 1948). The whole skeleton is never affected.

Signs and symptoms—The typical syndrome has been described above. Attention may be called to a case by any of the following: excessive thirst and polyuria, asymmetry of the face or prominence of one or both eyes, retardation of growth and infantilism, and swelling over a lesion in the skull or mandible. A cranial swelling may be soft, fluctuant and pulsatile; the defect in the skull may be actually palpable. If such a swelling is aspirated a culture is sterile. Stomatitis and gingivitis may occur early and may result in the teeth falling out, leaving granulomatous masses exposed. Pain connected with a bone lesion is exceptional and when present is mild. Diabetes insipidus is extremely common. If the petrous is affected deafness may result. Foul discharge from the ears may be present. Yellow pigmented areas on the skin are occasionally seen. In chronic cases papular eczema-like eruptions are fairly common and have been found to contain foam cells (Snapper 1949). Fibrosis of the lungs may first attract attention. Adiposity and hypogenitalism occur occasionally. As a rule the

spleen is normal but it has been found enlarged. Involvement of the mandible associated with diabetes insipidus but without radiographic changes in the skull, has been reported by Hankey (1938).

Blood examination reveals nothing characteristic. Occasionally there is some leucocytosis and in a few cases eosinophilia. Gross and Jacox (1942) in eighty four cases found thirteen with eosinophilia amounting to anything from 3 to 7 per cent. The blood cholesterol is normal or only slightly raised; only in exceptional cases is it materially increased, and then it may amount to 400 milligrams per cent. The serum calcium, plasma phosphorus and alkaline phosphatase are all normal.

Radiographic appearances—The typical osseous lesion is a sharply outlined, clear rounded defect. The most striking and suggestive lesions are seen in the skull in which, in a typical case, more than one punched-out hole of different sizes are seen. Usually one or two are larger than the rest and geographical in outline. As a rule there is no sclerosis around the clear holes but there may be later. Involvement of the base may be obvious. The holes may increase in size and new holes may appear. The outer table seems more affected than the inner in some cases. There may be fine mottling in addition, and in the very exceptional cases with no typical holes this may be the only change in the skull. In the long bones clear lesions are seen in the shafts, not in the epiphyses as a rule. They are endosteal and usually the cortex is not distended. There is no surrounding sclerosis except in the healing stage (Schüller 1939). Bowing of a bone is unusual but may occur. Only occasionally is a lesion fluffy and not sharply defined; such a lesion in the neck of the femur may be suggestive of a tubercular focus. Coarse trabeculation may be present and the appearance like an osteoclastoma; this was so in a case reported by Hansen (1949) but the child's age made an osteoclastoma improbable. In the spine a lesion may cause collapse of a body, and the appearance may then be that of Calvé's disease of the spine (Davies 1940). The case reported by Fawcitt (1942) with two vertebral bodies affected by what appeared to be Calvé's vertebra plana and with other skeletal lesions might well be one of Hand-Schüller-Christian disease. In a case reported by Jansson (1935) there was a paravertebral shadow surrounding two affected vertebrae strongly suggestive of a tubercular lesion. Mottling of the lungs has been seen. There is no generalised osteoporosis.

Progress—The course varies but generally it is inclined to be slow and benign. A lesion may heal, the hole in a bone becoming partially or completely obliterated according to its size. This may occur spontaneously or as a result of treatment by curetting or radiotherapy, but a lesion may recur. Sooner or later, however, a considerable number of the cases end fatally, often from intercurrent disease. In fatal cases the heart, large vessels, lungs or brain may be found involved. Statistics published by more than one observer indicate that about a third of the cases have proved fatal.

Complications—In one case a lesion in a femur was of sufficient size to call for amputation (Heinle 1934). Spontaneous fractures are rarely met with.

Pathology—If a lesion is reasonably fresh it will show on section yellow areas with dark patches caused by old haemorrhages. Histologically there is seen granulation tissue resulting from proliferation of the reticulo-endothelial cells and histiocytes. Some of the histiocytes have taken up cholesterol esters and become the characteristic foam cells. In the older lesion more fibrosis occurs, giant cells appear and the foam cells become increasingly scarce. There is no fibre bone formation (Falconer *et al.* 194?). If only one lesion is examined and foam cells are scarce it may be mistaken for polyostotic fibrous dysplasia. The skull lesions are extra-dural.

Diagnosis—The diagnosis depends on the whole clinical picture. If cranio-hypophysial lesions happen to be absent the diagnosis becomes very difficult and will depend on the result of a biopsy; in such a case it is advisable to select for biopsy a new lesion if possible. In myelomatosis the skull lesions are usually smaller and more numerous than those in this

disease while Bence Jones protein may be found in the urine. Carcinomatosis has given rise to difficulty but this can only occur in an exceptional case which should be above the usual age for Hand-Schüller-Christian disease. In hyperparathyroidism the skull changes are quite different: there is generalised decalcification of the skeleton and the serum calcium is raised. Symmetrical fenestra may occur in the parietals as a result of developmental error but these cause no symptoms and radiologically are unlikely to give rise to difficulties. An hereditary and familial incidence has been observed (Hallbertsma 1940).

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CASE 141—HAND-SCHÜLLER-CHRISTIAN DISEASE

(Figs. 404 and 405.) P. K., female aged three and a half years. Attended hospital for scaly rash on trunk (seborrhoeic dermatitis). Four months later was admitted with extreme anaemia. Very thirsty. Purpuric rash over whole trunk. Soft swellings present over the left parietal and the occipital. Holes in the skull readily felt. No enlarged glands. Spleen enlarged, and both spleen and liver easily palpated. Severe hypochromic anaemia. Hb 2. per cent. Leucocytes 12,600. Lymphocytes 56 per cent. Mantoux and Wassermann tests negative. Serum calcium 9·7 milligrams, plasma phosphorus 3·3 milligrams per 100 cubic centimetres. Alkaline phosphatase 5·1 units. Weight 20½ lb. Radiographs showed typical punched-out holes of various sizes in skull, and lesions in both femora, two ribs, the left radius and possibly the left ulna. Died about three weeks after admission in spite of blood transfusion. Lipoid infiltration found in brain, spleen and other organs. Dura infiltrated in parts. (Under Dr E. A. Cockayne.)



Fig. 404
Case 141—Skull showing typical multiple lesions of various sizes. The base of the skull is affected and the sella distorted.



Fig. 405
Case 141—Femora showing a sharply defined cyst-like lesion in both shafts.

CASE 142—HAND-SCHÜLLER-CHRISTIAN DISEASE

(Fig. 406.) I. S., female, aged five years. When three years of age suffered from urinary infection and whooping cough. Now has loss of appetite and is not gaining weight. Polyuria for past three months. Papulo-necrotic lesions of skin of trunk. Infected eczema of scalp. Bilateral otorrhoea. Head large. Exophthalmos, particularly of right eye. Few small glands in neck. Abdomen distended. Liver large. Spleen not felt. Blood examination revealed no anaemia. Serum calcium 10.3 milligrams, plasma phosphorus 4 milligrams per 100 cubic centimetres. Alkaline phosphatase 10.8 units. Blood cholesterol 1[illegible] to 200 milligrams per 100 cubic centimetres. Radiographs showed definite clear lesion in the anterior part of base of skull involving the orbits. Sections of two of the skin lesions showed no evidence of foam cells. (Under Dr. R. Lightwood.)



Fig. 406.

Case 142.—Skull showing some general fine mottling and a clear lesion of the sphenoidal region of the base. Note the involvement of the sella and the posterior part of the orbits.

CHAPTER 39

LETTERER-SIWE DISEASE

Reticulo-endotheliosis

This very uncommon condition is met with in infants and may be regarded as an acute form of Hand Schüller-Christian disease with a short and rapidly fatal course in most cases and without the secondary deposits of cholesterol esters in the cells of the granulomata. Though in most cases destructive lesions in the skeleton are present the soft tissues particularly the viscera, are chiefly affected. It has been reported under a variety of long names. Useful descriptions have been published by Jaffe and Lichtenstein (1944) and Snapper (1949) Three cases are reported by Schafer (1949) It usually affects children under two or three years of age and seldom those over four years.

The cause is probably an infection of some kind. Lesions are found in the liver spleen, glands lungs, skin and, in most cases, the skeleton particularly the skull. The thymus may be extensively invaded in cases showing bone lesions (van Creveld and Ter Poorten 1935) There is low fever and progressive anaemia. The liver and spleen are enlarged. Eruptions usually purpuric, occur and may progress to ulceration. Empyema may develop. Purulent otitis and mastoiditis have occurred in some cases. The skull is the most common seat of lesions but usually some other bones are also affected. The hands and feet are typically not affected.

The radiographic appearances may closely simulate those of Hand Schuller-Christian disease. If the base of the skull is involved, the characteristic symptoms of this latter disease *exophthalmos and diabetes insipidus may develop though the lesions are still without foam* cells. In a case shown to the author by Professor A. Moncrieff the metaphyses of many of the long bones were the seat of lesions which gradually increased in extent, with erosion of the cortex. The metacarpals and phalanges showed marked decalcified areas at both ends of the shafts.

All the lesions may be silent or one or two may provoke symptoms. In most cases death ensues within a few weeks of the onset, but in exceptional cases the child may live for a year or two. Pathologically the lesions are of two kinds, nodular and diffuse (Jaffe and Lichtenstein 1944) The nodular lesions are found particularly in the lymph glands but also in the spleen thymus, alimentary canal, skin and bone marrow Similar lesions have been reported in the lungs where the diffuse type of lesion is more common (van Creveld and Ter Poorten 1935) The diffuse lesion is also found in the dura, in the periosteum overlying a nodular focus and in the heart pancreas and kidney The bone marrow may be extensively affected even when destructive lesions are few Histologically the lesions in the bones may be indistinguishable from the early stages of eosinophilic granuloma with eosinophils prominent while later in the rare chronic cases, the lesions become more fibrous and display foam cells, and in fact approximate to the findings in Hand-Schüller-Christian disease.

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CHAPTER 40

GAUCHER S DISEASE

This disease i characterised by enlargement of the pleen a sociated with changes in some of the bones both being the result of infiltration of cells with a lipoid called kera in Described by Caucher in 188? it has been known by his name for many years In 1940 Chalmers estimated the number of reported cases at approximately two hundred Bone changes were first described by Pick (10**) Useful accounts of the disease have been reported by Hoffman and Makler (1020) who reviewed eighty nine cases Chalmers (1040) and Snapper (1949)

Hereditary and familial influences—It i frequently familial but only occa ionally inherited It has been reported in three generations

Sex—Females are more often affected than males

Age—It usually makes its appearance in childhood often in the third or fourth year but it may appear much later symptoms being delayed even until middle age One case was discovered a week after birth (Siegmund 10*1) Sixteen per cent of the cases reviewed by Hoffman and Makler were one year old or younger and 40 per cent under twelve years

Etiology—There seems to be general agreement that the cause is an inborn error of metaboli m the fault being congenital This results in the deposit of a cerebroside kera in in cells of the spleen and certain other soft tissues and in the marrow of the bones. Though Jews are specially affected the disease is by no means confined to them

Signs and symptoms—The condition is manifested by splenomegaly hepatomegaly moderate generalised lymphadenopathy pigmentation of the skin pingueculae haemorrhagic diathesis changes in the bones hypochromic anaemia leucopenia and thrombocytopenia. The out standing sign in most cases is enlargement of the spleen which may reach an enormous size It is said to enlarge downwards rather than downwards and to the right the usual direction except in young children (Tennent 104) The liver is also commonly enlarged but not to the same extent Ascites is seldom present, and jaundice is even more uncommon As a rule the progress is very slow but occa ionally in an infant the disease runs a malignant course with cerebral lesions nuchal rigidity opisthotonus and paralytic signs In spite of the enlargement of the abdomen the general condition is good The superficial lymphatic glands are not as a rule enlarged even though typical cells could be found within them but the internal glands and also the tonsils may be swollen A striking feature often present consi ts in brownish sub-conjunctival thickenings which are wedge-shaped with the bases at the inner side of the cornea these so-called pingueculae are seen almost exclusively in the older patients Pigmentation of the skin may be present. Thannhauser (1040) published an excellent coloured picture of a case with bilateral pingueculae both inside and outside each cornea and pigmented patches on the face Symmetrical pigmentation of the legs was stressed as a feature by Tennent (1945) Purpuric spots may be seen Malar flush and myopia have been noted in some cases. By some the disease is divided into two forms the visceral and the osseous, according to the tissues in which the lesions predominate In the osseous form there are said to be more blood changes and anaemia (Tennent 104?) In the visceral type with the splenomegaly predominating the only osseous change may be enlargement of the lower thirds of the femoral shafts Pains in the affected bones may be a prominent symptom particularly in the lower limbs the sternum and the spine Kyphosis may result from collapse of a vertebral body Exceptionally swelling and tenderness of a bone may be fairly acute and the clinical picture may then suggest osteomyelitis or arthritis. A mild degree of dwarfism may occur but this is unusual The lungs and kidneys are affected only quite exceptionally Invasion of the lungs by affected mediastinal glands may occur (Myers 1937) Typical Gaucher

cells have been found in sputum (Merklen *et al.* 1933). Deafness has been reported. A tendency to haemorrhage is common, particularly epistaxis and bleeding from the gums, petechiae, menorrhagia and haemoptysis may occur.

Blood examination—There is anaemia, and also leucopenia, in which it differs from Niemann-Pick disease in which leucocytosis is usually present, at least in the later stages. There may be a relative lymphocytosis. Leucocytosis may develop after splenectomy. Biochemical examination reveals no striking change. Kerasin cannot be demonstrated in the blood.

Radiological appearances—The most frequent change is an enlargement of the lower half or third of the femoral shafts, so that the normal trumpet shape is lost—a condition likened to an Erlenmeyer flask. The cortex is decreased in thickness and there is irregular reduction in density, giving rise to a mottled or streaky appearance. There is no sign of periosteal reaction. In the other bones the lesions vary considerably but the essential change is reduction in density by the presence of masses of Gaucher cells; there may be mottling, spotty decalcification or more gross cyst-like changes. Apart from the deformity of the femora mentioned already, there is no enlargement of the shaft of a bone as a rule. Seldom is the cortex ruptured. Only very occasionally is a really large osseous lesion met with. A more or less cystic lesion of unusual size in the lower end of a femur in a lad of seventeen years was reported by Potter and McRae (1933). The lesions are much less defined and sharply cut than those in Hand-Schüller-Christian disease. Sclerosis is exceptional, but it has been seen in a vertebral body and also in the tarsal scaphoid (Arkin and Schein 1948). Sclerosis and periosteal reaction were seen in the femur of a girl of twenty-one years in whom the heart was affected and the appearance of the humeral shafts was more suggestive of myelomatosis (Reed and Sosman 1942). In a case with the lungs fibrotic, the shaft of one femur was thickened and sclerotic with only a small clear central cavity. We have seen irregular increased density in the lower parts of the femora. The bones most frequently affected after the femur are the pelvis, the upper end of the humerus, the vertebrae and mandible. The skull very seldom shows any change; fine mottling was present in one case. There is no general decalcification of the skeleton. Cartilage is not affected, but joint surfaces may become involved. When the head and neck of the femur are affected the appearance may suggest aseptic necrosis as seen in pseudo-coxalgia or in caisson disease (Schein and Arkin 1942, Arkin and Schein 1948). Collapse of a vertebral body may occur (Buxton 1935). The bones of the hands and feet are seldom affected.

Progress—Except in the occasional malignant case met with in infants, the course is usually slow and may extend over several decades. Death usually results from intercurrent disease, but towards the end there may be some cachexia. Improvement following removal of the spleen has been reported, but the operation only relieves the patient of a "tumour" of great size and is not curative of the disease, though it possibly diminishes the anaemia for a time.

Complications—Spontaneous fracture at the site of a lesion has been reported, but this is uncommon. Changes simulating osteochondritis of the femoral head have already been referred to.

Pathology—The essential change is the infiltration of reticulum cells and histiocytes in the spleen, liver and other situations, including the bone marrow, with kerasin resulting in the formation of Gaucher cells. The Gaucher cells are large, with the cytoplasm marked by wavy parallel lines; situated usually near the periphery of the cell there are one or two small rounded nuclei with a nucleolus (Hoffman and Makler 1929). In the bone lesions the cells may be spindle-shaped. Degeneration and necrosis of the proliferating cells may occur, and when cancellous bone is extensively infiltrated fragments of the trabeculae may be involved in the necrosis; scarring and even calcification of the necrotic tissue may be observed (Weinmann and Sicher 1947). Cushing and Stout (1939) report a case in which sequestra were removed

from the acetabular floor during an operation Typical cells have only recently been demonstrated in the nervous system (Snapper 1949)

Diagnosis—The presence of an enlarged spleen or the scar produced by its removal should suggest the correct diagnosis when a cyst like lesion is discovered in a bone The leucopenia should also suggest this disease rather than other causes of splenomegaly In a case running an unusually rapid course Niemann Pick disease in which there is leucocytosis and no visible bone changes will have to be excluded An osseous lesion has been mistaken for osteomyelitis In one case a low grade staphylococcal arthritis of the hip joint was suspected at first (Cushing and Stout 1928) The possibility of changes in the hip suggestive of Perthes disease being due to Gaucher's disease should be kept in mind The flask like enlargement of the lower portion of the femoral shafts combined with changes in the texture of the bones should be definitely suggestive but leukaemia must be excluded. In a doubtful case in place of a biopsy sternal or iliac puncture may give conclusive evidence of Gaucher's disease Splenic puncture is more reliable but is not entirely free from risk, particularly in a case with haemorrhagic diathesis and it has therefore been largely discarded Parsons and Ebbs (1940) reported a girl of fourteen years with clinical evidence of the osseous form of Gaucher's disease but which proved post mortem to be due to multiple cavernous angiomata affecting the liver and spleen gland thymus mediastinum lungs kidneys and most of the bones.

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CASE 143—GAUCHER'S DISEASE

(Figs. 407 to 411.) Miss B. C., aged twenty-nine years. Attended hospital for pain and swelling of left knee. Pain not severe. Enlarged spleen removed three years ago. Soft, ? fluctuant swelling just above left knee joint. Some thickening of lower end of femoral shaft. Looks a normal healthy woman. Radiographic examination—skull shows fine mottling and undue translucency of the outer table, but no definite lesions. Spine shows general osteoporosis. L.4 body is increased in density except near upper surface which is clear as if hollowed out. L.3–4 disc is narrowed. Clear lesions in L.3 body. Texture of sacrum and pelvis is abnormal with many clear areas, mostly small. Advanced osteoarthritis of both hip joints. Upper femora show some distortion of surface and multiple small clear areas, particularly the right. Lower femoral shafts show characteristic enlargement with loss of the normal trumpet shape, some irregularity of the surface and somewhat streaky decalcification above the condyles. Mid-shaft of left femur is definitely cystic with subperiosteal new bone formation. Tibiae porotic and the middle two-fourths of each are cystic with curious cross-streaks of denser bone. Hands show subnormal density of the bones with some abnormality of the texture of the first and fifth metacarpals of the right hand. (Under Mr E. H. T. Hambly.)

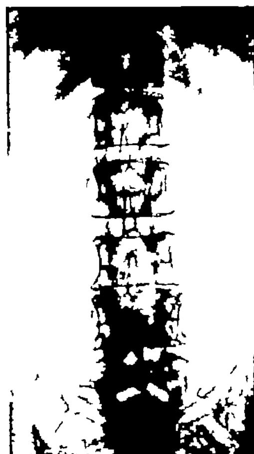


FIG. 407

Case 143. Lumbar spine showing general subnormal density except L.4 which shows increased density [illegible] its lower two-thirds or more and narrowing of L.3–4 disc. Note irregular texture of sacrum and ilia.



FIG. 408

Case 143—Lateral view of lumbar spine showing hollowing out of upper surface of L.4 body which is otherwise increased in density. Note the subnormal density of L.3.



Fig. 409
Case 143—Pelvis and upper femora showing cyst-like changes in all bones, periosteal thickening of the femora, particularly the left, and arthritic lipping in both hip joints.

Fig. 410
Case 143—Femoral shaft, showing characteristic abnormal shape and ill defined decreased density of the lower third, and endosteal cystic changes, with periosteal reaction in the middle third.





Fig. 411
Case 143—Legs showing the general decreased density of the bones, with cyst-like changes in the middle portions of the tibial shafts.

CASE 144—GAUCHER'S DISEASE

(Figs. 41? to 414.) D. B., boy aged nine years. In hospital for abscess in neck three years ago when enlargement of spleen and liver was noticed. Full investigation revealed nothing of importance. Always been fit and well. Splenectomy by Mr Charles Donald a year ago. Sternal puncture revealed no Gaucher cells. Haematemesis on one occasion only. Pain in left hip and limp began a few months before the splenectomy. Radiographs showed nothing abnormal. Joint aspirated and yellow opalescent fluid withdrawn; penicillin injected. Pain disappeared for several months but has now returned. Limp has increased. On admission—can walk without much difficulty. Left great trochanter is prominent; movements generally restricted, especially flexion. No shortening. Wasting of thigh muscles. Liver much enlarged. Blood examination at various dates: R.B.C. 7 000 000 to 3 100 000; W.B.C., 16 000 to 8 400. Cholesterol 123 to 140 milligrams per 100 cubic centimetres. Alkaline phosphatase 7 to 18·6 units. Radiographs show gross irregularity and fragmentation of the left femoral head and irregular decalcification of the neck extending to the great trochanter which is involved. Lower shafts of femora show definite suggestion of the typical deformity. Skull shows fine mottling with some areas of decalcification in the occipital region and near the site of the anterior fontanelle. (Under Mr Denis Browne.)



FIG. 412
Case 144—Hip joints showing advanced changes on the left. Note the fragmentation and partial destruction of the femoral head and the irregular clear areas in the neck extending down the outer side to the trochanter.



FIG. 413
Case 144—Femoral shaft, showing the abnormal shape of the lower third.

FIG. 414
Case 144—Skull showing the fine mottling in the frontal region and the lea... in the ...ital



CASE 145—GAUCHER'S DISEASE

(Figs. 41 and 416.) H. S. male aged thirty years (1944). Said to have had splenectomy performed in 192. when eleven years old. Subacute arthritis of knees and ankles in 1936. Acute rheumatism in 1931. "Dislocation" of right hip 1939. Deep radiotherapy to knees, right hip and both femora during past ten years. On admission—right hip adducted with limitation of movement. Signs of loose bodies in left knee. Radiographs showed gross irregularity in shape and subluxation of head of the right femur and in size and density of the neck and trochanteric region with lipping and other changes in the acetabulum. Lower thirds of both femoral shafts show typical Gaucher changes. Left knee shows changes suggestive of osteochondritis dissecans of the femur and of old healed fracture (? pathological) in upper third of tibia. Left knee operated upon and four loose bodies removed. Aunt of patient had splenectomy performed at age of twenty-six years.
(Under Sir R. Watson-Jones.)



FIG. 415
Case 145—Right hip showing subluxation and gross changes in the joint and also changes in the neck and trochanteric region of the femur.



FIG. 416
Case 145—Femoral shafts showing the characteristic alteration in shape and texture of the lower third or more of both.

CHAPTER 41

FLUOROSIS

Fluorosis is the name given to a form of generalised increased density of the skeleton with pitting and other changes in the teeth resulting from prolonged ingestion of fluoride of calcium, and is found in those working in cryolite a compound containing fluorine sodium and aluminium (Møller and Gudjonsson 1932) A similar condition was found in those living in the phosphatic zones of Morocco Tunis and Algeria (Spéder 1936) Changes in the teeth and skeleton of certain animals particularly cattle occur in these and other countries, the condition being known as El Darmous. More recently the affection particularly the changes in the teeth has been found in human beings in many parts of the world. Certain industries which distribute fluorine in their effluents have been the source of outbreaks not only in the workers but in cattle grazing in the neighbourhood of the works. Silicosis is present in half the affected workers according to Wilkie (1940) who reported two cases of generalised fluorosis the first to be recorded in this country A monograph on Fluorine Intoxication has been published by Roholm (1937)

In this country for some years past attention has been directed to the changes in the teeth in districts where the drinking water contains an unusual amount of fluorine. An outbreak of fluorine poisoning among cattle grazing near brickworks—the first outbreak in this country—was investigated by Bosworth and his co-workers (1941) The teeth of human beings and cattle show pitting and mottling, brown staining and a tendency to wear In children the changes are seen usually from the sixth to the twelfth year The brownin — or patches of brown stain—occurs later than the pitting and affects only part of the anterior surfaces of the front teeth (Sainsbury *1946*) In man the changes in the bones vary as might be expected with the degree of intoxication and the length of exposure and consist of increased density and subperiosteal thickening especially at points of attachment of muscles and ligaments. The bones first affected are the pelvis vertebrae and ribs. The jaws may be affected later The proximal parts of the long bones are more affected than the distal which may show no change in density The surface of the ribs may be remarkably spicular Since the condition takes time to develop marked petrosis in the contaminated regions is not usually seen before the age of forty-five to fifty It is suggested that the estimation of the fluorine content in the urine may be of value as an indication of danger (Green 1940) Calcareous deposits may be found in the vessels, ligaments within the cranium and even in the bladder wall The X ray appearances differ from those seen in marble bones in the surface of the bones being fluffy or spicular or occasionally even grossly thickened. There is no bone destruction as there is in osteoplastic metastases from carcinoma (Hunter 19[illegible]0) In the vertebral bodies there may be a suggestion of three zones two dense separated by a less dense band as often seen in marble bones.

The skull may be thickened In parts of China, where fluorosis is endemic, spondylitis leading to complete rigidity of the whole spine from skull to sacrum has been found (Lyth 1946) Specimens of affected spines showed generalised irregular outgrowths of bone from the vertebrae and ribs with calcareous deposits in the ligaments

Occasionally increased fragility may be present multiple spontaneous fractures having occurred in some affected animals. On analysis fluorine and calcium is found in excess in the bones which are said to be friable and crumbly Bosworth found in cattle the medullary cavity enlarged and filled by red gelatinous marrow osteomalacia and new bone on the surface

Symptoms may be present in the form of pains in the bones and joints cramps, wasting and loss of weight Anaemia and stomach troubles may be present (Møller and Gudjonsson 1932)

CHAPTER 42

OSTEOSCLEROSIS DUE TO BISMUTH, LEAD AND PHOSPHORUS

Dense transverse bands are sometimes seen in the radiographs of young growing bones, somewhat similar to those seen in mild cases of osteopetrosis but due to the ingestion of bismuth, lead or phosphorus. The bands occur in the metaphyses close to and parallel to the epiphysial cartilages; there may be two or more parallel bands. They are distinctly broader than lines of arrested growth. The rest of the bone is normal in appearance. In time they gradually fade or at any rate become obscured. According to Caffey (1937) they have been seen, even double bands, in a foetus whose mother had been under treatment with *bismuth*. If bismuth and arsenic are given for syphilis, he says, the arsenic produces the bands, which do not appear when arsenic is administered alone.

In the case of *lead* poisoning, it is the ends of the metaphyses of the more rapidly growing bones only which are affected (Vogt 1930). The bands are said to contain excess of lead, but the increased density is attributed to sclerosis of the bone (Park, *et al.* 1931). An epidemic of lead poisoning due to inhalation from the fumes produced by the burning in a stove of battery casings is reported by Cooper (1947); he reviews the whole subject and discusses the various possible sources of the poison.

Phosphorus in excess may produce similar but more striking bands. Bands half an inch wide may be seen in the metaphyses, while the density of the epiphyses may also be increased. In a case reported by Gottesleben (1930) two or more parallel dense bands formed curious arches in the upper ends of the femora, circles in the tarsal bones and in the epiphyses, and double transverse lines near both upper and lower surfaces of the vertebral bodies. Faint bands may disappear but well marked bands are never completely eradicated (Holm 1942). It should be remembered that dense bands in the metaphyses may be seen in cretins and also in infantile myxoedema.

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CASE 146—OSTEOSCLEROSIS DUE TO BISMUTH

(Fig. 417.) B. D., male, aged sixteen years. Has been under treatment in V. D. Department for congenital syphilis by intramuscular injections of bismuth. Complaining of some pain in region of knee joints. Radiographs show bands of abnormal density in the metaphyses, most marked in the neighbourhood of the knee joints. Similar though less dense bands of varying depth are also seen along the crests of the ilia, around the periphery of the femoral heads and condyles, and along the upper and lower surfaces of the vertebral bodies. (Under Mr A. B. Pain.)



Fig. 417

Case 146—Knees showing broad bands of increased density in the metaphyses of the femora and tibiae fading off towards the shafts. Narrow bands outlining the condyles are just visible.

CHAPTER 43

ENDOCRINE ERRORS

The skeletal changes that may result from endocrine disorders can be roughly classified as follows. Overgrowth of bone either in the form of excessive stature or overgrowth of certain parts of the skeleton is seen in pituitary gigantism, acromegaly and hypogonadal gigantism. Acceleration of growth followed by premature fusion of the epiphyses so that finally the stature is below rather than above the average, is seen in hyperfunction of the adrenals and of the gonads and also in Cushing's syndrome when the onset occurs in childhood. Dwarfism combined with a varying degree of sexual and mental infantilism, is met with in cretinism, cachectic infantilism, pituitary dwarfism (asexual ateleiosis) progeria, and also in some cases of Fröhlich's syndrome and occasionally even in Simmonds' disease, if the onset is sufficiently early. The effect on the stature in all these conditions whether towards increased or diminished growth naturally depends on the age at which the particular endocrine error becomes effective, the earlier the onset the more profound the effect on the skeleton. Fusion of the epiphyses is indefinitely postponed in hypogonadal gigantism and is also delayed, but without leading to excessive growth in pituitary dwarfs, cretinism, Fröhlich's syndrome and Simmonds' disease.

Generalised osteoporosis which combined with fibrocystic changes is seen so strikingly in hyperparathyroidism is also met with in hyperthyroidism, Cushing's syndrome, Simmonds' disease and in a type of premature senility known as Werner's syndrome.

Though not the result of an endocrine error it will be convenient to consider the sexual type of ateleiosis with the asexual.

PITUITARY

Hyperpituitarism—Pituitary Gigantism

This form of skeletal overgrowth results from hyperpituitarism which has developed before normal growth has been terminated by fusion of epiphyses to shafts. It corresponds to acromegaly in adults, a condition into which it merges and with which it is not infrequently combined even before growth has ceased. Many pituitary giants are acromegalic.

A *familial* tendency is certainly present in some cases.

Sex—Both sexes are affected.

Age—The onset is usually at about puberty but it may be earlier. Schlesinger (1931) reported a female "giant" of eight years with some acromegalic features.

Etiology—As in acromegaly the cause is hyperpituitarism associated with an eosinophilic adenoma of the anterior pituitary.

Signs and symptoms—The chief feature is excessive growth, more obvious in the limbs than in the trunk. The span is greater than the height which is said to have even exceeded 9 feet. We have seen a lad whose height was 6 feet 2 inches at the age of thirteen years. Though usually symmetrical, cases of hemihypertrophy or of more limited overgrowth have been reported. Facial asymmetry has also been seen. Traub (1939) reported the case of a boy of six years with generalised gigantism and arachnodactyly with excessively long big toes, a peculiarity which we have seen occasionally with other types of developmental error of the skeleton. As a rule muscular development is not increased to the same extent as the skeletal growth. Even when a giant is muscular at first, weakness sets in later. Round shoulders are common. When muscular development is excessive the appetite is enormous (Cawadias 194). Sexual development may be normal but it is more often subnormal and may be

reduced to complete sterility eventually even though at one time there may have been some precocity The earlier the onset the more likely is pubertas praecox to accompany the advanced statural development A tendency to feminism has been reported (Gilford 1911) Mentally pituitary giants are inclined to be subnormal sooner or later Headache may be complained of Splanchnomegaly corresponding to the degree of skeletal overgrowth is the rule

Radiological appearances—Epiphysial ossification may be advanced but in most cases fusion of epiphyses and cessation of growth take place at the normal times If the gonadotrophic hormone is deficient fusion of epiphyses may be delayed. The sella may be enlarged or distorted but is often normal

Progress—There is a strong tendency to the development of signs of acromegaly even before growth has ceased. Simpson (1938) says 40 per cent of giants of this type develop acromegaly Sternberg (1893) found fourteen acromegalics among thirty four giants Resistance to infection is low and life is often cut short frequently by tuberculosis. As in acromegaly there may be a transition to hypopituitarism eventually with senilism and cachexia

***Complications**—In Traub's case already referred to there was irregular ossification in a* femoral head and of some of the other epiphyses which he regarded as epiphysial necrosis he refers to two other somewhat similar cases. Diabetes may be a complication (Crooke 1948)

Pathology—Though an eosinophilic granuloma is usually present the only change may be excess of eosinophil cells. Occasionally the pituitary has shown no abnormality There may be either hyperplasia or hypoplasia of the thyroid and of the adrenal cortex The thymus may be large.

Diagnosis—This condition must be distinguished from hereditary gigantism which is seen more often in certain races, *e.g* Swedes. Eunuchoid gigantism should be distinguishable without difficulty

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CHAPTER 44

ACROMEGALY

In this condition characteristic changes in the face involving both the bones and the soft parts, enlargement of the hands and feet and splanchnomegaly develop as the result of hyperpituitarism. First described by Marie in 1886 its connection with the pituitary was pointed out by Minkowski in 1887 The literature is voluminous—the following articles are valuable stepping stones Cushing (1927) a monograph based on 1,319 cases by Atkinson (1932) and Knaggs (1935) In 1938 Wakeley and Atkinson found another 245 cases.

Hereditary and familial influences. Though not inherited, it is certainly familial in some cases. Jews and Swedes appear to be particularly susceptible

Sex—Both sexes are affected, males rather more often than females.

Age—It occurs with the greatest frequency in the third decade. It may begin in adolescence and occasionally in childhood, when it is associated with gigantism Atkinson in 1931 found twenty four cases under fifteen years of age. In one of these, gigantism began at the age of six years and the child was completely acromegalic at sixteen (Walker 1897) Schlesinger (1931) reported a girl of eight years with gigantism and acromegalic features.

Etiology—The cause is hyperpituitarism associated with eosinophilic adenoma of the anterior lobe of the pituitary

Distribution—The bones usually affected are those of the hands and feet, the mandible and skull. In the long bones changes are less frequent and less marked. Soft tissue changes are seen in the face, hands and feet and also in the viscera.

Signs and symptoms—The onset is insidious. The facial changes attract the attention of relatives the patient is worried by having to purchase increasing sizes of gloves and shoes. Headache, ocular-motor paresis, amenorrhoea and paraesthesiae are other possible initial complaints. Headache may be a severe symptom. The features generally become heavy the brows are accentuated, the skin is thickened the lips, nose and ears are enlarged and the lower lip is everted. The face is often described as negroid it may be oedematous. The lower jaw is enlarged and projects, so that normal occlusion of the teeth is impossible The reverse deformity with the upper jaw projecting has been reported (Crooke 1948) The length of the face is increased. The tongue is almost invariably enlarged, with the papillae prominent, and it may protrude. The zygomatic arches, the malars and the external occipital protuberance are enlarged. The voice is deep and resonant. Occasionally the scalp is sufficiently redundant to become wrinkled in parallel folds (Dott and Bailey 1925)—a condition sometimes described as bulldog scalp Exophthalmos is not uncommon. The hands and feet are enlarged and slowly increase in size but not indefinitely The fingers are thickened clubbed and cyanosed. The bones as well as the skin and subcutaneous tissues are responsible for the abnormal size which may be further increased by oedema. The thickening ceases at the wrist Excessive sweating may be complained of The fingers may be lengthened, particularly if the disease has been preceded by gigantism. The feet show similar changes and are increased in length. The shoulders are broad the clavicles being long and thick. Apart from the hands and feet the limbs show little if any change but osteoarthritis is common The antero-posterior diameter of the chest is increased. Kyphosis in the upper dorsal region is common and scoliosis may also be present If preceded by gigantism the cases are above the average in height Many giants become acromegalic Sternberg (1895) found fourteen of thirty four giants were acromegalic. One case with features of both conditions grew two inches between the ages of twenty nine and thirty five years excessive growth began at thirteen years and

after a few years ceased a fresh outburst of growth occurred at the twenty ninth year. The condition of the epiphysial discs is not referred to in the report of the case (Werner 1914).

There is general splanchnomegaly involving the liver, spleen, heart and lungs. The appetite may be large. The thyroid was enlarged in 44 per cent of the 1,064 cases studied by Wakeley and Atkinson (1938). Polyuria and polydipsia may develop in the later stages. At first the muscular power is increased, later there is a tendency to weakness and adiposity. With the development of increased intracranial pressure nervous symptoms may develop such as ocular palsies of various types, pain in the distribution of the fifth nerve, loss of smell and occasionally optic atrophy. The sufferers may become apathetic, listless and sullen, and the memory may deteriorate. Amenorrhoea and impotence may occur early and are constantly present later, even though in the initial stages there may have been some hypergonadism, which is most likely to occur when the onset of the disease is unusually early. In a female the uterus may be enlarged, in a male some hypertrophy of the external genitals may occur but this is followed later by atrophy of the testicles, sometimes accompanied by a tendency to feminism. Cases vary in the tissues chiefly affected, in some the bones, in others the skin and subcutaneous tissues, and in yet others the viscera show the greatest amount of change. Usually, but not invariably, the changes are approximately symmetrical.

Blood Examination—There may be eosinophilia, and sometimes hyperglycaemia. The latter may change to hypoglycaemia with increased tolerance. Glycosuria may occur. Dott and Bailey (1925) found it present in 20 per cent., and Simpson (1930) in 50 per cent. of the cases studied. In half of Simpson's cases the glycosuria was due to true diabetes.

Radiological appearances—The most striking changes are seen in the skull and mandible. There is prominence of the supra-orbital ridges with enlargement of the frontal sinuses. There may be some general thickening of the skull, particularly at the vertex and the occipital protuberance, but the chief thickening is of the zygomatic arches and malars. Sometimes the calvaria is thin. The alveolar ridge and palate may be thickened. The sella is usually but not invariably enlarged. The foramen magnum is altered in shape. The mandible almost invariably shows particularly striking changes. It is both enlarged and lengthened. By absorption of bone the angles become more obtuse. The symphysis protrudes. The arch formed by the body is enlarged and the rami are increased in length. The changes in the bone may be asymmetrical. The lower teeth become separated, but Keith (1911) maintained the alveolar ridge is not increased in length. The bones of the hands and feet are enlarged, especially at their extremities, and all surface markings are accentuated. There is tufting of the terminal phalanges. The carpal and tarsal bones may be enlarged. Putman and Davidoff (1938) maintain that squaring of the heads of the radii and the changes in the hands are diagnostic features. The major long bones show less obvious changes as a rule, but all surface markings are accentuated, and irregular enlargement of the ends, with exaggerated osteoarthritic lipping, is often seen. Osteophytes extending into tendons and ligaments are mentioned by Putman and Davidoff. Occasionally there appears to be actual lengthening of the bones and the stature is increased after all normal growth has ceased. The patellae may be enlarged, as occurred in a case reported by Wakeley and Atkinson (1938). The vertebral bodies are increased in size by additional bone, particularly on their anterior surfaces; a lateral radiograph, especially of the dorsal vertebrae, may show marked increase in the horizontal diameter of the bodies, while an antero-posterior view shows little abnormal except lipping. The spinal canal is not seriously encroached upon as a rule. H. L.-C. Wood's case (Case 147) is exceptional in this respect. The costo-chondral junctions are enlarged and exhibit irregular density (Wame *et al.* 1040). A case with cystic changes in the great trochanters and in the bones in the region of the knee joints was reported by Chester and Chester (1940). In the final stages of a case general osteoporosis may be seen.

Progress—Increase in the changes may be fast or slow, with or without remissions or exacerbations; the disease may remain stationary for years. Progress may be rapid when

the tumour of the pituitary is malignant There may be a gradual change to hypopituitarism, with signs of Simmonds disease

Complications—Diabetes mellitus has been mentioned already

Pathology—Besides the eosinophilic adenoma of the anterior lobe of the pituitary there may be polyglandular enlargement. In addition to the thyroid already mentioned the parathyroids may be enlarged occasionally with an adenoma. The adrenal cortex may be hyperplastic, and again there may be an adenoma. The thymus and lymph glands are large The condition of the pancreas varies. The ovaries and testes sooner or later become atrophic. Examination of the bones confirms the radiological findings. The additional bone on the surface of the vertebral bodies has been clearly demonstrated. The changes in the skull were intensely studied by Keith (1911) Cushing and Davidoff (1927) reported the finding of a liver twice and the kidneys three times their normal size The stomach was four or five times the normal size while the intestines measured twice the normal length. The lungs were also increased in size Wakeley and Atkinson (1938) found the brain enlarged. The heart and large vessels may also be abnormally large. Histologically the additional subperiosteal new bone is more irregular than normal bone. Hunter (1898) found increased vascularity of the marrow and cancellous bone including the diploë of the cranium. There is hypertrophy of the skin and subcutaneous connective tissues. In the arthritic joints Erdheim (quoted by Knaggs) found the changes begin on the deep surface of the articular cartilage and not on the joint surface but later the cartilage ulcerates and the changes soon become indistinguishable from those of osteoarthritis

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CASE 147—ACROMEGALY

(Figs 418 to 422) J T male aged forty six years Sustained a blow over right orbit thirteen years ago lost right eye Within eighteen months was becoming acromegalic Changes in the skull hand feet and chest progressed rapidly for eleven months with pains in back and legs. On admission complained of severe pain down front and back of right leg to ankle relieved by rest No headache Face definitely acromegalic but mandible not protruding Skin of face thick and coarse Chest markedly prominent anteriorly Spine rigid and kyphotic Right leg wasting of thigh straight leg raising to 80 degrees (left to 90 degrees) knee jerk diminished ankle jerk present no sensory loss Hands and feet large without obvious changes in the soft tissues. Blood nil abnormal Wassermann negative Lumbar puncture 10 millimetres. Cerebro-spinal fluid normal Radiographs showed marked prominence of the supra-orbital ridges with enormous enlargement of the frontal and other sinuses Sella irregularly enlarged Spine showed in the dorsal region considerable increase in the antero-posterior measurement of the bodies with marked lipping Laminectomy performed laminae of L.4 and 5 removed The two neural arches were thickened sufficiently to narrow the spinal canal. L. 5 1 disc was soft and bulging so some nuclear material was removed Dura opened sacral roots found to be excessively elongated loose and folded in coils as if the spine had been considerably diminished in length Section of bone removed showed normal cancellous bone containing cellular marrow Operation was followed by great relief of pain in leg Stiff lumbo-sacral corset supplied (Under Mr H L-C Wood)



Fig. 418
Case 147—Photographs showing the coarse features, the exaggerated supra-orbital ridges, and the marked prominence of the chest.



Fig. 419
Case 147—Skull showing the striking enlargement of the sinuses, with prominence of the supra-orbital ridges Distortion of the sella is visible



Fig. 420



Fig. 421

Case 147 Figure 420—Anterior view of skull showing the gross enlargement of the frontal sinuses, and some thickening in the malar regions. Figure 421—Dorsal spine showing the enlargement of the bodies anteriorly with marked arthritic lipping



Fig. 422

Case 147—Hands, with normal hand for comparison showing general slight enlargement more marked th right

CASE 148—ACROMEGALY

(Figs 423 and 424) C W I male aged forty seven years About fifteen years ago noticed the articulation of his teeth was faulty The mandible hands and feet have increased in size gradually ever since Has had to purchase increasing sizes of hats and shoes Some headache but not severe Has had difficulty in obtaining satisfactory dentures and inquired whether something could be done to reduce the size of the lower jaw Face typical nose thick ears heavy and stiff Lower jaw prognathous thick and wide right ascending ramus is longer than left chin displaced to left Hands and feet decidedly large and clumsy Eyes normal Radiographs showed prominent supra-orbital ridges increase in the sinuses prominence of the occiput and typical changes in the shape of the mandible The usual changes in the hands and feet were seen



Fig. 423

Case 148—Skull showing the pneumatisation of the sinuses thickening of the occiput and elongation of the mandible with alteration of its angles.



Fig 424

Case 148—Hand showing enlargement of the bones with accentuation of the markings, and tufting of the terminal phalanges

CHAPTER 45

CUSHING'S SYNDROME

Pituitary Basophilism

This condition which usually affects women is characterised by a rapidly acquired plethoric adiposity hypertrichosis, amenorrhoea and advanced osteoporosis of the skeleton. It was described by Cushing in 1932 a useful account of it was published by Crooke (1946)

Sex—It affects females far more often than males.

Age—It is usually seen in early adult life and only exceptionally in childhood or adolescence. Farber *et al* (1943) collected twenty-six cases under sixteen years of age and added one of their own.

Etiology—The cause was thought by Cushing to be invariably a basophil adenoma of the pituitary but it is now known to result also from adrenal cortical hypoplasia or neoplasm and from tumour of the thymus. Common to all cases whatever the primary cause is hyaline change in the basophil cells of the anterior pituitary (Crooke 1935) The sella is rarely enlarged.

Signs and symptoms—The adiposity develops rapidly and affects the face neck and trunk but not the limbs. Not infrequently there is considerable pain associated with it. The face becomes a dusky plum colour Amenorrhoea is accompanied by virilism with hypertrophy of the clitoris, and hypertrichosis of the male distribution The scalp hair becomes thinner while a beard and moustache appear and additional hair grows on the limbs pubis and in the axillae. Purplish striae on the abdomen and pigmentation are common The heart is enlarged and the blood pressure raised. Diabetes mellitus with polydipsia, polyuria and decreased sugar tolerance may occur Excretion of 17 ketosteroids in the urine is increased with a basophil adenoma but to a much greater extent when an adrenal is responsible

A "peculiar softening" of the bones has been found at autopsy The osteoporosis is particularly marked in the pelvis, spine and ribs. In a lad of fifteen years Farber *et al* found the generalised osteoporosis was particularly marked in the skull. Kyphosis is common Males are seldom affected in them impotence and feminisation occur When the condition begins in childhood there may be skeletal precocity at first but rapid growth is eventually stopped by premature fusion of the epiphyses. Muscular strength may be considerably increased for a time Initial sexual precocity gives way to suppression in such cases the disease may well be mistaken for the adreno-genital syndrome at first Enlargement of the thyroid may occur Over-activity of the parathyroids has been suspected as the cause of the osteoporosis, but the serum calcium is not raised though the excretion of calcium is increased. The porosity of the bones is due to deficient formation of matrix resulting from lack of protein and not to disorder of calcium and inorganic phosphorus metabolism (Albright *et al* 1941) Crush fracture of a vertebral body and more or less spontaneous fractures elsewhere in the skeleton may occur

Sooner or later increasing weakness gradually sets in and the sufferers eventually succumb usually within five years or so of the onset

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CHAPTER 46

HYPOPITUITARISM

Pituitary Dwarfism

Lorain type of Infantilism

Ateleiosis (Asexual)

In this condition dwarfism and infantilism are due to deficient secretion of the anterior lobe of the pituitary. This type of infantilism was described by Lorain in 1871. Ateleiosis (incompleteness) is the name suggested by Gilford (1907).

Sex—Both sexes are affected.

Age—It may begin in foetal life, but growth is usually normal for the first two or three years. Signs of arrested growth most frequently appear from the second to the ninth year (Cockayne 1937).

Etiology—The commonest cause is probably a tumour or cyst of Rathke's pouch.

Signs and symptoms—The signs are dwarfism of the short limbed type in some cases and of normal proportions in others, and sexual infantilism. Mentally the cases vary, some are childish and rather backward, but others are quite intelligent. Facially they are inclined to be remarkably alike. The voice is high pitched. The hair on the scalp is fine and scanty and that on the body deficient or absent. Marked freckled pigmentation of the face of a pituitary dwarf of thirteen years was reported by Werner (1934). The present writer has seen a case with a large pigmented area on the forehead and scalp. Eruption of the permanent teeth is delayed. The milk teeth are retained to an unusual age, occasionally both deciduous and permanent sets are retained together. There is delay both in the appearance of the epiphysial centres and in their union with the shafts, in some cases non union is permanent. A calcified suprasellar cyst may be seen. An enlarged and deformed pituitary fossa in one of these cases was first described by Levi (1908), but radiographic evidence supporting the diagnosis of pituitary disorder is quite exceptional (Bronstein and Cassorla 1946). The prospect of life is below normal, they are inclined to age prematurely. Polydipsia and polyuria have occurred as complications. 17-ketosteroids may be decreased in the urine (Rowlands and Simpson 1949). These authors reported the case of a pituitary dwarf of forty three years who passed into a condition of Simmonds' disease, his bones becoming osteoporotic. There is an absence of normal proliferation of cartilage at the epiphysial discs (Gilford 1907).

Ateleiosis (Sexual)

This type of dwarfism is present at birth and accounts for many of the midgets who perform in troups. It is distinguished from the asexual type by the normal sexual development.

The cause is entirely unknown. Only very rarely has it been inherited, but it may be familial.

The features are inclined to be babyish and these dwarfs are remarkably similar in appearance. The dwarfism is of the short limbed type. Puberty occurs normally but may be delayed and if this is so epiphysial fusion may also be delayed. The sella is normal. The bones are radiographically normal except for their size (Brailsford 1944).

These dwarfs may live to old age. They are usually intelligent and capable of earning a living. If they have children the latter are normal. Gilford (1911) reports the case of a male sexual ateleiotic whose son was a dwarf of the asexual type.

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CASE 149—ASEXUAL ATELEIOTIC DWARF

(Fig. 425.) A. T., female aged thirteen years. First child. No miscarriages. Cut first tooth at nine months. Sat up at end of first year, walked at three and a half years. Learnt to talk late. Thought at first to be myxoedematous cretinism. Refused solid food even at six years; teeth very bad. At seven years radiographs of hips suggested healed Perthes disease. Sella diminished in size and deformed. Height 31 inches (normal [illegible] inches). Head large. Limbs disproportionately short. No signs of sexual development. (Under Dr R. Lightwood.)

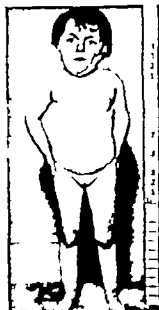


Fig. 425

Case 149—Photograph at thirteen years showing general appearance. Note the relatively short legs and the large head and childish face.

CASE 150—ASEXUAL ATELEIOTIC DWARF

(Figs. 426 and 427.) A. L., male aged forty-six years. Attended hospital for injury of left forearm. Radiographs revealed fractures of the radius and ulna and ununited epiphyses of these bones at the wrist. Fracture treated for six months without obtaining union. Height 4 feet. Weight 80 lb. Perfectly proportioned dwarf—leader of a midget troupe. Intelligent. Voice high pitched. Has worn glasses for thirty years for myopia. No headaches. No polyuria. Radiographs show calcified cyst of the pituitary with ballooning of the sella. Facial bones comparatively small. Frontal sinuses minute. Epiphyses of the pelvis and in the region of the elbow joint united, and possibly the femoral heads, though the epiphyseal lines of the last are still visible; all other epiphyses examined are ununited. (Under Mr St. J. D. Buxton. British Journal of Surgery, 1939, 27, 181.)



Fig. 426



Fig. 427

Case 150. Fig. 426—Skull showing enlarged sella with calcified cyst projecting upwards. Note the small size of the frontal sinuses. Fig. 427—Wrist and part of hand showing all epiphyses visible in film are ununited.

CHAPTER 47

DYSTROPHIA ADIPOSO GENITALIS

Fröhlich's Syndrome

This condition is characterised by adiposity and backward sexual development associated in some cases with dwarfism and mental infantilism. It was first described by Babinski in 1900 and a year later a case was published by Fröhlich with whose name the condition is generally associated. The descriptive title was suggested by Bartels (1908). An excellent account of this and other types of hypopituitarism was published by Langdon Brown (1936).

Hereditary and familial influences play no part in the incidence.

Sex—Both sexes are affected.

Age—It occurs most frequently about puberty but signs may appear earlier particularly a tendency to adiposity. Occasionally the onset is delayed.

Etiology—The whole pituitary gland is faulty. Though the hypoplasia may be primary it is usually secondary to a cyst or tumour pressing on the gland. Chromophobe adenoma of the gland has been described in adult cases. Hydrocephalus has been responsible in some cases. Congenital suprasellar cyst of Rathke's pouch is said to be the commonest cause in children (Cockayne 1947).

Signs and symptoms—Adiposity is invariably present. The fat accumulates particularly about the limb girdles and extends down as far as the elbows and knees; the distribution in the legs has been likened to "plus-fours" (Langdon-Brown 1923). Fat also accumulates on the back and under the breasts. The genitals are infantile. There is amenorrhoea in females and undescended testicles in males. In male cases developing after puberty atrophy of the external genitals occurs. Dwarfism may be present of the short-limb type if it begins before the second dentition (Gardiner Hill 1937) but this never becomes extreme and is often absent. The voice is high pitched. Somnolence is common. There may be hypotonia of the muscles with laxity of the ligaments. Moderate polycythaemia may be found. Radiographs may show the pituitary fossa enlarged or distorted but it is often normal. Fusion of the epiphyses may be delayed but without excessive growth. Some cases have antecedent hyperpituitarism, with precocious puberty and early fusion of epiphyses. Occasionally signs of intracranial pressure develop with disturbance of vision. Polyuria and polydipsia may occur. Atrophy of the thyroid is occasionally present.

Adolescent coxa vara, slipping epiphysis, is frequently seen associated with signs of Fröhlich's syndrome usually in boys; as a rule these lads with coxa vara show no tendency to dwarfism. The growth cartilages are said to be thickened and this renders the epiphyses unstable. Though other changes in the hip joint have been described in association with Fröhlich's syndrome slipping of the femoral head is the only one which has developed sufficiently frequently to be of clinical importance.

Most cases of Fröhlich's syndrome become mature eventually though they may retain their tendency to adiposity. Adiposity and hypogenitalism occur occasionally in Hand-Schuller-Christian disease.

The following two allied syndromes have been recognised.

Burnier's syndrome in which dystrophia adiposo-genitalis is associated with marked dwarfing and optic atrophy is the result of a slow-growing tumour often a teratoma, pressing on the pituitary (Cockayne 1947).

Laurence-Moon syndrome in which obesity and hypogenitalism are associated with mental retardation, retinal pigmentation, polydactyly and in some cases dwarfism. It is a familial disease; in no case has the complete syndrome been inherited. This is a congenital disease for which the pituitary is not responsible. (Cockayne *et al.* 1935; Sorsby *et al.* 1939.)

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CHAPTER 48

PROGERIA

This condition named by Gilford in 1904 was described by him in 1911 as manifested by the rapid advance of old age in one who is in a conspicuous state of defective development." Signs of infantilism are followed by those of premature senility the two conditions then being combined. Both elements in the syndrome vary with the age at the time of onset the earlier the infantilism appears the more pronounced the senilism later Atkinson (1937) collected fourteen cases. The onset is usually in infancy or early childhood. It is commonly but not universally ascribed to hyposecretion of the anterior lobe of the pituitary the result of a cranio-pharyngioma or ischaemic necrosis. Polyglandular errors are favoured by Atkinson to account for the condition. The photographs of the published cases are singularly alike. The clinical picture is that of a dwarf with the wizened features of old age. A thin peaked nose thin lips, small mandible prominent staring eyes scanty white hair narrow shoulders, feeble muscles, wrinkled skin, and large knuckles make up the picture. Ossification is said to be in advance of normal for the age rather than backward and arthritis is common (Crooke 1948) In the skull, at any rate, ossification is deficient and delayed Sexual development is delayed. Arterio-sclerosis is found post-mortem. In a girl of fourteen years, said to be a typical case decalcification of the skeleton was extreme she is reported as having had no less than four sets of teeth (Exchaquet 1935)

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CHAPTER 49

SIMMONDS DISEASE

Pituitary Cachexia

This condition is characterised by cachexia and premature senility and for many years has been regarded a due to deficiency of the anterior lobe of the pituitary with secondary degeneration of the gonad thyroid adrenals and pancreas If as occasionally happens it commences in childhood it merges into progeria in fact Simmonds disease is regarded by many as the adult form of progeria (Cawadias 1047) It usually affects women particularly post partum when labour has been complicated and accompanied by profuse haemorrhage

The cause is said to be ischaemic necrosis infective infarcts cyst formation or fibrosis of the anterior pituitary only occasionally has a tumour been found Destruction of the eosinophil cells may be the only pathological change (Langdon-Brown 1030) It may follow acromegaly

The clinical picture of Simmonds disease is that of premature senility The sufferer becomes thin and anaemic with a low blood pressure and slow pulse There is loss of weight The mandible atrophies and the teeth are lost The fingers become tapering and delicate There is gonadal atrophy with amenorrhoea and loss of pubic and axillary hair Diabetes insipidus may occur The viscera are reduced in size The basal metabolic rate is lowered There may be relative lymphocytosis and sometimes eosinophilia.

The skeleton shows no characteristic change but osteoporosis, as might be expected, certainly may occur (Rowlands and Simpson 1042) The pituitary fossa is distorted or enlarged. This is regarded as essential for the diagnosis of Simmonds disease by Fraser (1948) who also described certain tests for non-gonadotrophic pituitary insufficiency Progress is downhill and may be rapid.

If the onset is in childhood the condition varies with the age of onset and the severity of the case There is cachexia and the facies become senile Varying degrees of dwarfism and infantilism develop the former being of the short limbed type if the onset is sufficiently early Fusion of the epiphyses is delayed and may never occur There is little hair and no sexual development. The excretion of 17 ketosteroids is decreased. In 1939 Sheehan on the study of fifty-one cases, maintained it was a misconception that most cases of Simmonds disease have cachexia, but this view does not appear to have been generally accepted. In 1949 Sheehan and Summers studied ninety-five cases of " true hypopituitarism and stated that most cases diagnosed as Simmonds disease with emaciation and progeria have no significant lesion of the pituitary in their opinion many of the cases diagnosed as hypopituitarism are suffering from anorexia nervosa.

Werner's syndrome (1904) is a condition apparently allied to Simmonds disease though it is not due to an endocrine error the cause is unknown. Thannhauser who in 1945 reported four cases between thirty and forty years regards this condition as progeria of the adult. In this syndrome shortness of stature is combined with premature senilism, hypogonadism, dermatosis trophic ulcers juvenile cataract tendency to diabetes osteoporosis, metastatic calcification and calcification of blood vessels. It is said to exhibit a familial tendency

Cachectic infantilism and dwarfism—Infantilism and dwarfism may result from any chronic wasting disease that occurs during the growing period. The causes are such conditions as gastro-intestinal diseases with malnutrition chronic abdominal tuberculosis heart disease and tropical diseases such as malaria and dysentery The skeleton in cachectic dwarfism

presents no special features. Harris (1933) pointed out that in cases which have suffered severe infections in quick succession the partial suppression of cartilage growth may become complete with fusion of the epiphyses in early adolescence He would prefer the term premature senility to infantilism for such cases.

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CHAPTER 80

CRETINISM

This condition which results from congenital inadequacy of the thyroid is characterised by dwarfism and infantilism associated with a peculiar facies. Cretinism may be endemic or sporadic. The connection of the sporadic affection with deficiency of the thyroid was discovered by Fagge in 1871.

Heredity and familial influences—The endemic type occurs in affected families living where goitre is endemic. Sporadic cases occur anywhere and in any family.

Sex—Both sexes are equally susceptible.

Age—Though the defect in the thyroid is congenital, the child is not a real cretin at birth and will display no more than a suspicion of the affection until six or more months have elapsed, particularly if fed on the breast.

Etiology—Thyroid inadequacy is universally accepted as the cause.

Signs and symptoms—The onset is gradual. To the experienced eye the face or placidity of the child soon after birth may raise suspicions. In a typical case the head is large and the face strongly suggestive. The lips are thick, the mouth is open and the tongue protrudes, the slit like eyes are wide apart. The hands and feet are square and spade-like, cold and blue. The fingers are squat and equal in length. The muscles are feeble and the joints loose. The abdomen is large. There are pads of fat in the supraclavicular regions and over the vertebra prominens. There is general infantilism. Mentally they are backward and sleepy. Their movements are slow. Sexually they are retarded. They gradually develop dwarfism of the short limb type; they rarely exceed four feet in height. Treatment, even when given late, may result in additional growth. The temperature is inclined to be subnormal. Deafness is not uncommon. They may be myxoedematous.

Blood Examination—The alkaline phosphatase is very low; in the younger patients this is regarded as a reliable index by Le Marquand and Tozer (1943). There may be anaemia; the blood cholesterol may be high. There are no signs of a metabolic error.

Radiological appearances—Skeletal changes are more marked in sporadic than in endemic cases. In the skull the fontanelles are large and the closure of the sutures delayed. The base may be short. The long bones are short in proportion to the trunk and the muscular ridges are poorly marked. Dense bands are seen at the ends of the shafts, adjacent to the epiphyseal lines. Jupe (1938) published radiographs showing well-marked bands in infancy and complete disappearance of the increased density two and a half years later. The epiphyses are late in appearing and in fusing to the shafts. There may be stippling of the epiphysial centres, notably those for the femoral and humeral heads. These changes are bilateral, and are more likely to be seen when treatment has been delayed (Cockayne 1947). The final result may be considerable flattening of the heads of these bones. In the hip both the early changes and the final deformity may be indistinguishable from Perthes' disease. Brailsford (1944) refers to the "beaked femur" of cretinism. Permanent distortion of the joint surfaces in an adult cretin of thirty nine years is illustrated by Berard and Novel (1930). In the spine dorso-lumbar kyphosis, with one vertebral body smaller than the others, may occur (Kemp 1946). We have seen the typical spine of gargoylism in two cretins.

Progress—Progress varies even under efficient treatment. The outlook is better when treatment is commenced early. The face never becomes quite normal. The long bones are always short. The effect of treatment on the epiphysial changes appears to be uncertain; it cannot be relied upon to prevent permanent distortion of the joint surfaces.

Pathology—In endemic cases the thyroid may be enlarged though inactive. In sporadic cretins the thyroid is either fibrotic and atrophic or absent There is diminution of cartilage proliferation at the epiphysial discs. The marrow is said to be fatty and deficient in cellular ti ue and it may contain lymph follicles. Secondary diminution of eosinophil cells in the pituitary has been found and to this has been attributed the dwarfism.

Diagnosis—The gargoylism type of chondro-osteo-dystrophy is the condition most likely to cause difficulty particularly since the same spinal deformity may be met with in both. In gargoylism cloudy corneae enlargement of the liver and spleen and coxa valga are usually present Dense bands at the ends of the diaphyses are seen in phosphorus bismuth and lead poisoning and in some cases of osteopetrosis

INFANTILE MYXOEDEMA

Brissaud s type of Infantilism

Myxinfantilism or acquired myxoedema in childhood is said to be less uncommon than many think (Cockayne 104) It usually commences about the third or fourth year but may be later If the onset is before the second dentition short limbed dwarfism delayed fusion of epiphyses mental and sexual retardation are seen Ossification of epiphyses may be both delayed and irregular stippling of the epiphyses may be seen (Jewesbury 1938) Dense bands, similar to those seen in cretins may appear in the metaphyses.

HYPERTHYROIDISM

In Grave s disease a point of interest is the occurrence of generalised osteoporosis of the skeleton—thyrotoxic osteoporosis as it is called. Young women are much more often affected than men. It may occur at any age Multiple more or less spontaneous fractures may occur Extensive osteitis fibrosa in addition to osteoporosis has been reported (Askanazy and Rutishauser 1033 Jaffe *et al* 103?) In children the disease is uncommon especially before the age of ten years, though it may even be congenital There may be early ossification of epiphyses and premature development of the teeth skeletal growth may or may not be accelerated It occurs more frequently in girls. There is evidence that both familial and hereditary influences affect the incidence (Le Marquand and Tozer 1043)

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CASE 151—CRETINISM

(Figs. 428 to 430.) L. C., female, aged twelve years. Admitted to hospital for osteochondritis of both femoral heads. Has received a great deal of treatment for cretinism. An intelligent child. Skin coarse and pigmented. Movements of hips full in all directions. Blood cholesterol 350 milligrams, blood urea 8.5 milligrams per 100 cubic centimetres. Radiological examination showed delayed ossification of several epiphyses and of the carpus. Mottling of humeral heads. Hips showed mottling of right femoral head and gross fragmentation of the left, femoral necks thick, especially left. Bands of increased density seen in the metaphyses of some of the long bones and the metacarpals. Hips treated by rest and traction and later by caliper splint. Administration of thyroid continued. Two years later films show femoral heads are of uniform density with smooth articular surfaces but they are shallow and spread, particularly the left, in which the appearance is typical of healed Perthes' disease. (Under Mr E. S. Evans.)



Fig. 428

Case 151—Hips showing the abnormal ossification of the femoral head and the broad neck.





Fig. 429 | Fig. 430

Case 151. Figure 429—Wrist showing some delay in the ossification of the carpus, and of the radial and ulnar epiphyses. Note the increased density adjacent to the epiphyseal lines at the end of radial, ulna and metacarpal shafts, also the increased density in the centres and at the surfaces of the carpals. Figure 430—Hips after two years' treatment, showing the permanent changes in the femoral heads and necks.

CASE 152—CRETINISM

(Fig 431) V L., female aged two years. Apparently normal at birth Weight 7 lb. Could stand with help at one year been backward since Cannot yet walk. Eruption of teeth delayed till eighteen months. Two siblings older normal. Dull lethargic child Dry scaly skin with scanty hair Eyes widely separated. Mouth large with thick loose lips. Tongue large and protruding Only seven teeth present. Low dorso-lumbar kyphosis. Abdomen large Margin of liver low General muscular hypotonia. Blood cholesterol 250 milligrams per 100 cubic centimetres. Radiographs showed development of skeleton was generally backward. Skull large with widely open sutures sella slightly enlarged. Angular kyphosis is shown to be due to first lumbar body which is small abnormal in shape and displaced backwards, a condition strongly suggestive of that seen in gargoylism. (Under Dr R. Lightwood.)



FIG. 431

Case 152 —Lateral view of spine showing the abnormal shape of the bodies of L 1 and 2, with backward displacement of the small L 1 body

CHAPTER 31

GONADS

Both hyper- and hypo-activity of the gonads may affect skeletal growth but whereas hyperactivity is much more commonly seen in females, skeleton changes resulting from hypogonadism are almost exclusively met with in males. Ovarian hyperactivity may become apparent at any age in childhood, even in infancy. The cause is a granulosa cell tumour of low malignancy. The result is *Macrogenitosomia Praecox*, a condition in which there is acceleration of skeletal growth and sexual precocity. The precocious growth is terminated by premature fusion of the epiphyses, so the early tendency to gigantism ends in some degree of permanent dwarfism. There may be a tendency to obesity and increased muscular development. Dentition may be advanced.

Similar precocity in males, as the result of an interstitial tumour of the testis, is extremely uncommon. Excess of growth followed by early arrest, sexual precocity and abnormal muscular development occur.

HYPO-GONADAL OR EUNUCHOID GIGANTISM

In this condition skeletal overgrowth occurs as a result of gonadal insufficiency or suppression. The overgrowth is not as marked as in hyperpituitary gigantism, in fact the excessive stature is seldom worthy of the name of gigantism. Heredity plays no part in the incidence, nor is it usually familial, exceptions to this rule occurred in a family reported by Sainton (1902). It is almost exclusively a male affection. The onset is usually in adolescence but it may appear earlier.

Some cases have been below the average in height before the accelerated growth commenced. If the testicular inadequacy is only partial to begin with, the progress may be slow and the clinical picture incomplete until as late as the thirtieth year (Simpson 1948). The commonest cause is congenital hypogonadism, but the testicular inadequacy may result from infection, neoplasm or trauma of the testicles. In some cases the primary fault is in the pituitary.

The outstanding signs are abnormal stature and sexual infantilism. The testicles are frequently undescended. The epiphysial centres may appear late, their fusion to the shafts is invariably delayed, even for several years. The limbs are relatively long, the span exceeds the height. The hands are long and narrow and the fingers tapering. Dentition is retarded. Musculature is poor. Knock-knee and flat foot are common. Besides the delay in epiphysial fusion, radiographs show the cortices and trabeculae of the long bones less solid than they should be. The skull may be small and the sutures obliterated. The pituitary fossa is normal. The big toes were excessively long in a case reported by Werner (1942). 17-ketosteroids in the urine are said to be decreased. Mentally the cases are inclined to infantilism and feminism. They may be either thin or obese. In girls menstruation is delayed or scanty.

There is no tendency to acromegaly later as there is in pituitary gigantism.

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CASE 153—EUNUCHOID GIGANTISM

(Figs. 432 to 433.) R. M., male, aged twenty-eight years. Attended hospital for trouble in right knee. Kicked in lower abdomen at nine years; fainted. No further details obtainable. At nineteen years was told the lack of body hair and failure of the voice to break was due to non-descent of the testicles. At twenty years joined Army; passed A1. Few months later injured right knee. Was constantly reporting sick for pain in knee, fatigue, etc. Eventually discharged from Army with diagnosis of an endocrine error. Since his discharge has worked, but only intermittently, at light jobs. On examination, a very tall slim young man of adolescent appearance with a hairless face. Voice has not broken. Height 6 feet 3 inches. Flabby and frail. Body completely hairless. Skin white, soft and smooth. Hips inclined to feminine contours. Mentally adolescent. Testicles not felt even in inguinal region. Penis small. Muscle tone poor. Ligaments lax and joints hyperextensible, particularly the elbows. Eyes normal. Radiographic examination: skull shows normal sella, but hyperpneumatisation of sinuses. Non-union of epiphyses of vertebrae, lower ends of femora, both ends of tibiae and fibulae, upper ends of humeri, epicondyles, lower ends of radii and ulnae. The femoral heads, the epiphyses in the region of the elbow joints except the epicondyles, and the epiphyses of the metacarpals and phalanges are partially or completely united. Seen by Dr Raymond Greene, who considered the case due to testicular failure, though the remarkable pneumatisation of the sinuses suggested slight over-activity of the eosinophil cells of the pituitary. On his suggestion ten pellets of 100 milligrams each of testosterone were implanted in the abdominal wall. Response to treatment was remarkable. Within a couple of months his voice was breaking, hair grew on his face, pubic region and in the axillae, his skin thickened and became more masculine; sexually he became more normal. Psychologically he became more masculine and adult. (Under Mr E. T. Bailey.)

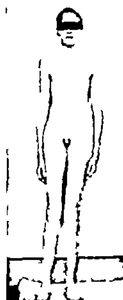


Fig. 432

Case 153—Photo at twenty-eight years showing the slim build, rather feminine hips and sexual infantilism.



Fig. 433

Case 153—Skull showing normal sella, but marked enlargement of the frontal sinuses and antra.



FIG. 434

Case 153—Hand and wrist showing non-union of the radial and ulnar epiphyses and incomplete union of several epiphyses in the hand at twenty-eight years.



FIG. 435

Case 153—Right knee showing non-union of the femoral and tibial epiphyses at twenty-eight years.

CHAPTER 52

ADRENALS

Adrenal hyperactivity is met with much more frequently in females than males and in them the condition produced is known as the *Adreno-genital syndrome*. The cause is simple hyperplasia with or without a cortical adenoma; only exceptionally is a malignant growth present. Adrenal hyperplasia may be secondary to a pituitary fault. Adolescence is the commonest period for its occurrence but both adults and young children may be affected. It is inclined to be familial and to attack certain races.

There is sexual precocity with masculination and, in adults, virilism. They become muscular like a male, acquire obesity of the male type and hypertrichosis which may include growing a beard and moustache.

If it begins early there is skeletal precocity followed by premature cessation of growth so the final stature may be below the normal. Dentition is advanced. Menstruation may begin early and soon cease or never commence at all. Mentally they correspond to their ages. In adults the only skeletal change and this only occasionally met with is osteoporosis (Spence 1937). The diagnosis from Cushing's syndrome may be difficult at first. In the presence of an adreno-cortical carcinoma the 17 ketosteroids in the urine are much increased, a point which distinguishes them from non-carcinomatous cases; an additional test of value, a colour test, was published by Patterson (1947).

In males a corresponding affection occurs extremely rarely, but it has been reported, even in infancy. Acceleration of skeletal growth may cease abnormally early and thus end in a certain degree of dwarfism. The picture is much the same as that resulting from testicular hyperactivity. There is sexual precocity and abnormal muscular development—the "Infant Hercules Type" of Weber (1920). Hemihypertrophy associated with pubertas praecox in a boy of six and a half years with an adeno-carcinoma of an adrenal was reported by Harwood (1932, 1933).

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CHAPTER 53

CONGENITAL OR INHERITED SYPHILIS

In this affection of infants infection with the spirochaeta pallida has occurred before birth. Admirable general accounts of the condition have been published by Dennie and Pakula (1940) and Nabarro (1949).

Hereditary and familial influence.—It is usually inherited from the mother but occasionally only the father shows evidence of the disease the mother being apparently healthy. Though in most cases the mother has a positive Wassermann, a considerable number of mothers have no clinical signs of syphilis.

Age.—Signs of the disease usually appear during the first six months of life most frequently in the third or fourth week but occasionally they are delayed many months or even for years. Only exceptionally are signs present at birth.

Signs and symptoms.—Early signs are rhinitis (snuffles) rashes and anaemia. An erythematous rash appears on the face forehead and buttocks whence it spreads to the abdomen and down the legs. It is common on the lips and chin and may be confined to these parts. Sores mucous tubercles and radiating fissures—rhagades—appear on the lips and are followed by scarring which may be a useful diagnostic sign later. Condylomata may appear about the anus but they are uncommon. The so-called café-au-lait face may develop. Cranio-tabes is not uncommon. Thickenings around the anterior fontanelle—Parrot's nodes—develop giving rise to the natiform or "hot-cross-bun" skull. Choroiditis iritis optic neuritis and interstitial keratitis may develop but the last is more commonly met with later. Convulsions hydrocephalus and cerebral diplegia may occur. The viscera are rarely affected in those who survive birth. Orchitis is seen in a small proportion of the cases.

Statements as to the frequency of skeletal complications are conflicting but they are certainly not uncommon at four to twelve weeks after birth. The ends of the long bones become enlarged and tender as osteochondritis develops. This is often called "syphilitic epiphysitis" though the metaphysis is the chief seat of the changes. The upper limbs are more often affected than the lower particularly the distal ends of the radius and ulna. An affected arm hangs flaccid by the side—Parrot's pseudo-paralysis. In the legs protective spasm is more common. Separation of an epiphysis may occur but the plane of separation is in the metaphysis not at the junction of metaphysis and epiphysial disc as in traumatic cases. Active osteochondritis is rarely seen after the fifth month (Fleigel 1949). The hands and feet are seldom affected. Syphilitic dactylitis may occur usually involving a proximal phalanx and spreading later to the metacarpal or metatarsal.

Blood examination reveals nothing characteristic except a positive Wassermann. A negative Wassermann is not conclusive evidence against syphilis (Nabarro 1949). Though some 40 per cent of the new born cases give a negative Wassermann there are few exceptions to the rule that by the third month the reaction is positive (Fleigel 1940). The E.S.R. is raised.

Radiographic appearances.—A clear band of considerable depth develops in the metaphysis close to but not quite at the end of the shaft. Between the decalcified zone and the epiphysial disc is a narrow denser line sometimes irregular or "saw tooth" the so-called "lattice" similar to that seen in scurvy. Radiographic changes may precede clinical evidence of local inflammatory changes. The cortex adjacent to the clear band becomes eroded this is common at the inner side of the upper end of the tibia and is regarded as of considerable diagnostic value by Nabarro and others. When both tibiae are eroded in this way the appearance is called Wimberger's sign (Fig. 3). Periosteal reaction occurs and subperiosteal shadows appear along the shaft. When an epiphysis becomes loose and displaced the line of cleavage occurs

in the decalcified zone the lattice being displaced with the epiphysis and disc as a result of a pathological fracture through the metaphysis. The skull may show osteoporotic mottling and fuzziness of the outer table and there may be many clear holes in which both tables are involved (Dennie and Pakula 1940). Gummatous lesions may appear in the bones, as illustrated by Wallace (1919). In syphilitic dactylitis a clear area is surrounded by dense sclerosis.

Pathology.—On section of a bone the lattice is seen macroscopically as a yellow irregular line it is caused by increased depth of the zone of provisional calcification. It may be irregular like the cutting edge of a saw at the end of the metaphysis. Rarefaction is seen in the adjacent clear band. Fibrosis of the marrow spaces is an important feature (Turnbull).

Diagnosis.—If osteochondritis occurs unusually early with flaccidity of an arm Erb's palsy may have to be considered. In birth palsy the position of the arm close to the side with the elbow extended and the whole arm markedly rotated inwards so that the palm faces outwards is characteristic. When osteochondritis occurs later scurvy may have to be excluded. It may also be mistaken for osteomyelitis or even poliomyelitis.

Secondary and tertiary complications.—When infancy is past an affected child may be undersized ill nourished, sallow and may display general infantilism, as in the case reported by Ellis (1932). The spleen may be enlarged and other viscera affected. The later types of bone change may occur any time after the third year (Nabarro 1949). Nodes may occur on the long bones or the skull as a result of osteoperiostitis. This commonly but not exclusively affects a tibia, frequently both tibiae there is smooth fusiform cortical thickening usually of fairly uniform density and involving a considerable length of the shaft, particularly the anterior aspect, producing the so-called " sabre tibia." This inflammatory change is associated with pain, particularly at night. Gummata may develop in the skin liver lungs, or in one or more of the long bones. Perforation of the palate or nasal septum may occur with permanent depression of the bridge of the nose.

Symmetrical effusion into the knees—Clutton joints—is the commonest type of joint affection. It is usually a simple synovitis with negative radiographs, and only rarely does a true arthritis develop. It may occur as early as the seventh year but usually later (Nabarro 1949). The so-called Hutchinson's teeth, seen in a quarter of the cases, refer particularly to the permanent upper central incisors. Normally the crown of this tooth often shows signs of having developed from three papillae or cusps which have been smoothed off to form a straight cutting edge. In congenital syphilis the central papilla is suppressed and the remaining two bend towards each other with the result that the cutting edge is narrower than the rest of the crown and may be notched. The lower centrals and upper laterals and canines may also be deformed. More important from the diagnostic point of view is the deformity of the first molar. The crown of this tooth is dome-shaped the cusps which should lie around the peripheral part of the biting surface have fallen towards each other and the sides of the tooth are thickened and convex.

The typical affection of the eyes is interstitial keratitis. Various types of neuro-syphilis may develop even juvenile general paralysis and tabes congenital tabes is mentioned by Dennie and Pakula (1940). We know of two cases in which Charcot joints developed in adolescence.

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CASE 155—CONGENITAL SYPHILIS

(Figs. 438 and 439) G S female aged nine weeks. Attended hospital for swelling of limbs. Radiographs showed typical syphilitic changes in the long bones. Fourteen months later found to have severe rickets. (Under Dr Donald Paterson)



Fig. 438

Case 155—Arm showing decalcification of the metaphyses with erosion of the cortex at the lower end of the radius.

Fig. 439

Case 155—Leg showing the decalcified band and the dense lattice in the metaphyses. Note the characteristic erosion on the inner side of the upper end of the tibial shaft.

Fig. 438 Fig. 439

CASE 156—CONGENITAL SYPHILIS

(Figs. 440 and 441) D H. male aged one month. Attended hospital with "pseudo-paralysis" of lower limbs. Definite clinical signs of osteochondritis at ends of several major long bones. Orchitis of right testicle. Wassermann markedly positive in both mother and child. Radiographs show typical syphilitic changes with evidence of fractures through some of the metaphyses and with signs of repair

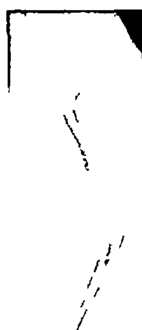




Fig. 440

Case 156—Left arm showing marked changes in the humerus with signs of periostitis throughout the shaft. At both ends new bone has been formed to repair metaphyseal fractures and stabilise the epiphyses.



Fig. 441

Case 156—Legs showing decalcification of the metaphyses and widespread periostitis. Separation of the ends of some of the bones has occurred, notably at the lower ends of the femora; signs of repair are visible

Fig. 440 Fig. 441

CASE 157. CONGENITAL SYPHILIS

(Figs. 442 and 443.) D. W., male, aged three weeks. Premature child. No other children, no miscarriages. Born with marked oedema of face and of all four limbs. Oedema disappeared in two or three weeks except from left leg. Mother has signs of secondary syphilis. Child has slight snuffles. Marked oedema of left leg which is tender; similar signs but less marked in right leg. Pseudo-paralysis of both legs and left elbow which is enlarged. Radiographs show widespread syphilitic changes. Wassermann negative, mother strongly positive. Developed jaundice. (Under Dr. R. Lightwood.)



Fig. 442

Case 157.—Legs four weeks after commencement of antisyphilitic treatment, showing the efforts at repair, particularly in the left leg, in which both femoral epiphyses have been detached and the lower displaced.

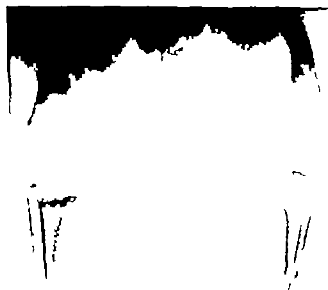


Fig. 443

Case 157.—Legs at age of ten months, showing almost complete cure of the bone changes seen in earlier films.

CASE 158—CONGENITAL SYPHILIS

(Figs. 444 to 448.) R. J male aged five and three-quarter years Eight months child. At four and a half months right arm hung limp regarded as a greenstick fracture. At three and three-quarter years said to have dragged the left leg which was painful along the shin the skin of which was shiny Nature of case still not recognised. Two years later admitted to hospital with pain in right leg and both arms. Joints not swollen or tender but left elbow was stiff and the external epicondyle was enlarged. Radiographs showed in several bones changes of two distinct types—sclerosing osteoperiostitis and osteolytic cyst-like lesions. The cyst like lesions regarded as gummata, were seen in the lower end of the left humerus the upper part of the right tibial shaft the left fibular shaft and possibly also the right. Nodes of dense cortical sclerosis were seen in the shafts of the left femur (two) right and left tibiae and left ulna. Wassermann strongly positive. Anti-syphilitic treatment given Six months later there were signs of healing of most of the lesions an exception was the gumma in the left fibula which was definitely larger After a further six months treatment this lesion had almost disappeared and the patches of cortical sclerosis were much reduced in size.



Fig. 444

Case 158—Legs (J ary 1929) showing two areas of sclerosing osteoperiostitis in shaft of left femur and similar changes in both *tibial shafts and in the left* fibula Gummata are seen in the upper third of the right tibia and left fibula and possibly in the upper metaphysis of the right fibula



Fig. 445



Fig. 446

Fig. 445
Case 158—Legs (July 1928) showing improvement in the sclerotic lesions and complete disappearance of the gummata in the upper end of the right tibia but extension of the changes in the left fibula

Fig. 446
Case 158—Left leg (February 1929) showing cure of the lesions is almost complete



Fig. 447



Fig. 449

Fig. 447
Case 158—Left arm (January 1928) showing gumma in lower end of humerus and osteoperiostitis of the ulnar shaft

Fig. 449
Case 158—Left arm (January 1929) showing cure of the lesions in the humerus and ulna is almost complete

CASE 159—CONGENITAL SYPHILIS

(Fig 449) F C. male aged eleven years. Swelling of right shin said to have followed a blow two months ago Typical signs of sabre tibia in right leg Left leg normal. No other signs of congenital syphilis. Wassermann strongly positive in mother and child.



Fig. 449
Case 159—Lateral and antero-posterior views of right leg showing typical osteoperiostitis of the middle portion of tibial shaft.

CASE 160—CHARCOT'S DISEASE OF HIP RESULTING FROM CONGENITAL SYPHILIS

(Fig 450) J W., female aged seventeen years. Was treated for epiphysitis" when two months old. Eyes bad since age of three and a half years. Father said to have sores on legs. Two sisters healthy No miscarriages. Slight limp for past five years Pain and limp in left hip one year following a fall. Treated as a tuberculous hip. Left hip trochanter raised flexion and abduction painful after 30 degrees of movement. Trendelenberg s sign positive. Leg 1½ inches short Ankles swollen. Bridge of nose depressed Choroiditis in both eyes. Wassermann positive. Knee jerks obtained with difficulty Ankle jerks not obtained. Radiograph showed gross changes in left hip strongly suggestive of Charcot s disease (Under Mr St J D Buxton. Case reported Proceedings of the Royal Society of Medicine 1923 (Orthopaedic Section 9) 19



Fig. 450
Case 160—Left hip showing gross changes in the acetabulum, with migration and considerable new bone formation and possible loose fragments Femoral bead has disappeared, the neck ending in a smooth straight line

CHAPTER 54

INFANTILE CORTICAL HYPEROSTOSIS

This affection of infants is characterised by the formation of subperiosteal bone on the shafts of the long bones and on the mandible. The first case was reported by Roske (1930). In 1945 Caffey and Silverman reported four cases including one previously published by Caffey (1930) and they suggested the title by which the condition is now generally known. Only five British cases appear to have been published (Ellis 1939, O'Reilly 1941, MacGregor and Davies 1949, Sakula 1950, Smitham and Palmer 1950). Excluding doubtful cases at least thirty have been reported.

Hereditary and familial influences—The mother of one case we know of is said to have had a similar affection but this could not be confirmed. Van Zelben (1948) reported a brother, sister and second cousin all with definite signs of the disease.

Sex—Males are affected more often than females in the proportion of three to one.

Age—The age of onset varied from foetal life to seven months the average being about two and a half months. Cases as old as two years and more have been reported but the true nature of these seems to us questionable.

Etiology—The evidence points to infection as the probable cause possibly a virus infection. In only one case was umbilical infection definitely recorded.

Signs and symptoms—Early signs have been swelling of the face (in nine cases) or of a limb or part of a limb. In two cases swelling in the scapular region occurred. In many cases irritability and fretfulness had been noticed. Fever was present at the onset in four cases. Soft tissue swelling is present in some in addition to the thickening of the bones and this swelling may occur quite rapidly. Clinical swelling of the bones or soft parts or both occurred sooner or later in at least twenty four cases. Tenderness of the swollen part may be present. In most cases several bones are affected in some practically all the major long bones are involved. The lesions are not necessarily symmetrical. The bones affected in order of frequency are the tibia humerus clavicle femur radius ulna, mandible (one or both sides) ribs fibula and scapula. The vertebrae hands and feet seem to be exempt and the calvaria almost so. The involvement of the face has been stressed the mandible was affected in nearly half the cases. Swelling may precede the appearance of radiographic changes. In one case the swelling of the face recurred on one side once and on the other on two occasions the last being when the child was five months old (Caffey and Silverman 1945). Redness and heat were never noted in the overlying skin. Fever was recorded in just over half the cases one case was feverish for as long as six months. In four cases complete absence of fever throughout was specially mentioned. Enlargement of lymphatic glands appears to be unusual. The spleen was enlarged in only one case. Proptosis occurred in one case pleural effusion was present in three. Chemotherapy appears to have no effect on the disease.

Blood examination—Anaemia was present in some transfusions were considered advisable in one case (O'Reilly 1949). Leucocytosis was noted in more than half the cases and was probably present in almost all. In some the alkaline phosphatase was increased, and in some the E.S.R. was raised.

Radiographic appearances—The first change is the appearance of a subperiosteal shadow enclosing a varying length of the shaft of the bone frequently the whole. The shadow may be smooth in outline or its surface may be lumpy to begin with but is never spicular. It may occupy only one side of a shaft at least in the early stages. It is often denser than the shaft

along which it has formed. The epiphyses are not involved. After a time the shadows cast by the new bone and the cortex blend, and the bone then appears to be increased in size and in density. Later still the dense cortex and new bone are partially decalcified and the appearance becomes that of an enlarged bone of subnormal density with a thin shell of denser bone beneath the periosteum. In time the enlarged porotic bone gradually shrinks and the shaft resumes its normal appearance. If a curvature has developed in the shaft this is slowly and spontaneously corrected. One or both tibiae developed a curve in at least five cases and the radius a curve in one case. There was still some abnormal curvature in both tibiae two and a half years after the onset in one case. There is some decalcification, probably only disuse atrophy in the unaffected parts of the bones. In one case the facial bones were affected and there was ossification in the tibio-fibular interosseous membrane at two points (O Reilly 1949)

Progress—Within a few weeks or months recovery sets in and is eventually complete. The average course is about eight months but it may be prolonged to two years. One arm was still swollen eight months after the onset and radiographs were abnormal at eleven months.

Pathology—Biopsy was performed in ten cases without providing much help in elucidating the cause. Only in two cases were there signs of inflammation in one of these the bone was affected (Kane and Borzell 1947) and in the other there were inflammatory changes and oedema of the muscles and periosteum (Dickson *et al* 194). Excess of osteoblasts was found by O Reilly (1949). Though no signs of active inflammation were found the marrow was fibrous and extremely vascular with a surprising number of osteoclasts present in a case recorded by Sherman and Hellyer (1950). Cultures have proved sterile.

Diagnosis—No doubt some cases have been mistaken for osteomyelitis, secondary to umbilical infection and operated upon. Osteomyelitis should not be as widespread as many of the cases of infantile cortical hyperostosis. The difficulty is increased by the fact that in infants osteomyelitis is less acute and less likely to progress to suppuration and necrosis than in older children. The age at which infantile cortical hyperostosis usually occurs should make scurvy improbable or impossible. Birth trauma would only call for consideration when the condition begins particularly early and is still confined to one bone. A condition of infants described as *hypervitaminosis A* may be associated with periosteal reaction on the long bones giving an appearance somewhat suggestive of infantile cortical hyperostosis: the differential diagnosis is discussed by Rothman and Leon (1948) who report three cases and refer to one published by Toomey and Morissette (1947). This condition affects children in their second year of life there is no fever and the response to correction of the dietetic error is rapid and conclusive.

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CASE 161—INFANTILE CORTICAL HYPEROSTOSIS

(Figs. 451 to 4 0.) H. J. female aged two months. Admitted for swelling of left leg present for past two weeks. Had mild umbilical sepsis for six weeks. Examination showed rounded swelling of left tibia not tender. Radiographs showed dense subperiosteal shadows on shafts of most of the major long bones on the right clavicle and the left scapula. Temperature 00 to 100 degrees. Various investigations of blood etc. all negative. Wassermann negative in parents and child. Further radiographs during following two and a half years showed fusion of the subperiosteal bone with the underlying cortices, rarefaction of the new and old bone, curvature of the tibiae particularly the left, and eventually a gradual return towards the normal shape and texture of the shafts. The return to normal of the tibiae was unusually slow and was still incomplete at the last examination. Child in hospital only for five weeks. Perfectly healthy appearance maintained throughout. (Under Dr P. Palmer.) (Case reported by Smitham and Palmer 10.0)



Fig. 451

Case 161—Left shoulder (August 1947) showing increased density of the scapula and subperiosteal shadow on the humerus

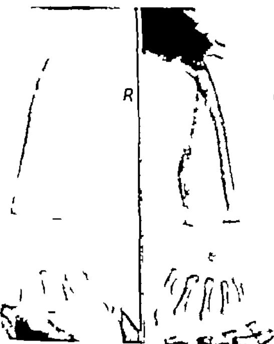


Fig. 45

Case 161—Forearms (August 1947) showing dense subperiosteal shadows on the radii and early changes in the ulnae



Fig. 453

Case 161—Arms (October 1947) showing changes in density of the periosteal shadows on the humeri and radii, further change in the right ulna, and partial decalcification of the cortices of some of the affected bones.



Fig. 454

Case 161—Arms (April 1948) showing the restoration of the bones to normal shape and texture is almost complete



Fig. 455

Case 161—Left leg (August 1947) showing dense subperiosteal shadow on the [illegible]. In the lateral view the mode of production [illegible] of at least part of the anterior [illegible] is clearly seen.



Fig. 456

Case 161—Legs (October 1947) showing both tibiae now affected. The outline of the subperiosteal shadow on the left tibia, which was *smooth*, has *now* become nodular and decalcification of the cortex has begun.



Fig. 457

Case 161—Legs (January 1948) showing the decalcification of the tibial cortex with blending of the new and old bone along the shafts. Note bowing of tibial shafts.

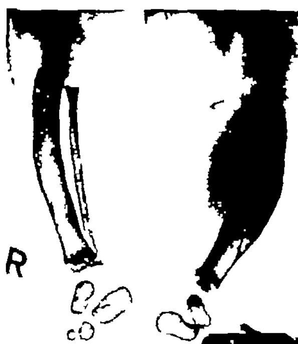


Fig. 458

Case 161—Legs (April 1948) showing the tibial shafts now appear to be enlarged and curved, and all signs of a subperiosteal layer of new bone have practically disappeared.



Fig. 459

Case 161 Legs (April 1950) showing restoration to normal of the tibial shafts is still incomplete two and a half years after the onset

For most of the ... are ... debted to the British Journal of Radiology which kindly lent the block

CHAPTER 58

HYPERTROPHIC OSTEOARTHROPATHY

This condition is characterised by clubbing of the fingers, periosteal thickening of the long bones including those of the hands and feet and polyarthritis and it is commonly but not invariably associated with pathological lesions in the chest. It was first described by Marie in 1890. In typical cases, often labelled Pulmonary Hypertrophic Osteoarthropathy, the new subperiosteal bone found on the shafts is smooth and a definite cause in the chest or elsewhere is discoverable. There is however another group of cases with clubbing of the fingers in whom the affected bones, particularly *the distal portions of the long bones of the forearms and legs* are rough, the chest is persistently normal and there is a distinct tendency to a familial incidence. The relative position of these two groups is in doubt but they certainly appear to deserve separate consideration. The better known Marie type will be considered first. Useful resumes have been published by Hunter (1940) and Tidy (1944).

Hereditary and familial influences play no part in the incidence.

Sex—It is distinctly commoner in males, the proportion to females being at least five to one.

Age—It occurs at all ages, most commonly in middle age—thirty to fifty years. It is uncommon in children. Wynn (1904) published a case of only eighteen months.

Etiology—In most cases it is secondary to disease in the chest; the conditions responsible include tuberculosis, fibroid lung, empyema, bronchiectasis and malignant disease of the lung, pleura and mediastinum. It may also follow congenital heart disease and infective endocarditis. Extra-thoracic causes include such chronic diseases as dysentery, pyelonephritis, alcoholism, polycythaemia rubra vera, hypertrophic cirrhosis of the liver, steatorrhoea and Raynaud's disease. The changes have been confined to one limb, the primary cause being an aneurysm. It is not always remembered that it may be secondary to an osteogenic sarcoma, the widespread bone changes sometimes occurring before any signs of thoracic metastases have been discovered. The present author has met with two such cases, the seat of the primary lesions being the tibia and radius. *There seems little doubt a toxin of some kind must be responsible for the* widespread bone changes. The part played by congestion in the production of the clubbing has been much discussed. Weber (1900) reported a case of Hodgkin's disease with typical signs of hypertrophic osteoarthropathy.

Signs and symptoms—The onset is gradual. Clubbing of the fingers is invariably present. The skin of the hands, feet and distal portions of the arms and legs may be thickened. There may be palpable thickening of the affected bones, particularly above the wrists and ankles. Dorso-lumbar kyphosis may be present. Symmetrical joint changes occur in about a third of the cases, particularly if very chronic. The affected joints are stiff and may be tender. Those near affected bones are most frequently troublesome, especially the knees, ankles and wrists. There may be exacerbations with a rise of temperature. Perspiration may be excessive. The signs may appear quite early when the condition *is secondary to carcinoma of the lung*.

Radiological appearances—Typically there is a layer of smooth new bone under the periosteum extending for a variable distance along the shaft of the bone. These changes are symmetrical. The bones affected are the metacarpals and metatarsals, the first two rows of *the phalanges, all the major* long bones and the scapula and patella. The skull, carpals and tarsals are usually normal. The new bone is not infrequently laminated, there being three or four parallel layers. The surface as a rule is smooth in this type of osteoarthropathy.

Progress—The condition itself has no effect on life. Affected joints may become eroded. If the chest condition is cured, simple clubbing may disappear entirely and the bone and soft

tissue changes may regress. Sometimes however no regression follows cure of the cause. Removal of a tumour from the thorax may be followed by regression even rapid regression only to be succeeded by a recurrence of the widespread changes if and when the tumour recurs.

Pathology—The bone changes are essentially ossifying periostitis. The additional subperiosteal bone consists of very vascular cancellous bone and the separate layers of this bone fuse later but remain recognisably separate from the cortex which may become somewhat decalcified (Compere *et al* 1935) In the joints synovial thickening occurs.

Diagnosis—The joint changes may be mistaken for polyarthritis due to other causes. If radiographs are taken and show typical changes on the surface of the adjacent bones there should be no difficulty about the diagnosis Ellman (1947) reported three cases due to carcinoma of the lung all referred to him as cases of atypical rheumatoid arthritis. Leukaemia can produce widespread subperiosteal shadows on the shafts of long bones including the ribs and may have to be considered when no primary disease can be discovered in the chest or elsewhere.

Idiopathic familial hypertrophic osteoarthropathy—The literature of this second and apparently allied group is confusing cases have been published under a variety of titles, e g Osteopathia Dysplastica Familiaris (Mankowsky *et al* 1934) Idiopathic Familial Generalised Osteophytosis (Freund 1938) and Chronic Idiopathic Hypertrophic Osteoarthropathy (Camp and Scanlan 1948) The onset is in adolescence or even in late childhood. The features which distinguish these cases from those in the other group are it is frequently familial there is an absence of changes in the chest or elsewhere to account for the condition and the subperiosteal new bone is irregular and spicular instead of being smooth on the surface. Clubbing of the fingers is present The skin above the ankles and wrists and to some extent of the hands and feet, is thickened and infiltrated. In some the skin of the face and scalp has also been thickened and wrinkled (Grönberg 1927) The bone changes may be widespread but are most common on the distal portions of the shafts of the tibia, fibula, radius and ulna, and correspond to the chief skin thickening Besides being irregular on the surface the additional bone tends to fuse with the cortex beneath it eventually producing an enlarged roughened bone of more or less uniform density In two cases at least there appears to have been a recurrence or exacerbation of the signs year by year (Freund 1938 Möller 1930) Involvement of the skull mandible ribs and clavicle in addition to all the long bones is described by Camp and Scanlan (1948) The joint changes may or may not be important. We had the privilege of examining a brother and sister affected by this type with Mr H H Langston who later showed one of them at the Royal Society of Medicine (1950) Absorption of the tufts of the terminal phalanges occurred in a girl of sixteen years (Weens and Brown 1945) bones which are unaffected in ordinary osteoarthropathy As a rule the condition causes no serious disability at least for several years.

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CASE 162—HYPERTROPHIC OSTEOARTHROPATHY secondary to SARCOMA OF TIBIA

(Figs. 400 to 401) D. I. female aged nineteen year. Admitted for pain in back for past five months, local swelling on back for past month. Left knee became swollen seven months ago. Two and a half years ago mid thigh amputation of right leg was performed for sarcoma of upper end of tibia, the tumour having been first noticed six weeks previously. Pathological report stated very malignant spindle-celled growth with much calcification but no ossification.

Examination revealed clubbing of fingers, swelling of small joints of fingers and of left knee with synovial thickening. Enlarged gland in left groin. Large hard swelling in left lumbar region extending into left side of abdomen. Rise of temperature occasionally. Radiographs of chest said to be negative. Widespread periosteal new bone formation involving practically every bone in the body except the vertebrae, ribs, carpus and tarsus. Died about seven weeks later. Autopsy revealed metastases in the right lung extending into liver. Mass in lumbar region and abdomen was retroperitoneal and had eroded some of the lumbar vertebrae. There was calcification in its wall. (Under Mr J. B. Hunter.)



Fig. 400
Case 162—Right leg (September 1930) showing sarcoma of tibia.



Fig. 401
Case 162—Forearm (May 1933) showing characteristic subperiosteal layer of bone extending the whole length of the radial and ulnar shafts.



Fig. 402
Case 162—Hand (May 1933) showing periosteal shadows on all bones except the terminal phalanges and the carpals.



Fig. 463

Case 162—Knee (May 1933) showing periosteal new bone on femoral and tibial shafts, and on the upper half of the patella. Note the new bone on the femur is laminated.



Fig. 464

Case 162—Leg (May 1933) showing involvement of the whole of the shafts of the tibia and fibula. In places lamination of the new bone can be seen.

CASE 163—IDIOPATHIC FAMILIAL HYPERTROPHIC OSTEOARTHROPATHY

(Figs. 465 and 467) D. S. female aged fifty-seven years. Said to have had enlargement of wrists and legs above the ankle and clubbing of the fingers since childhood. Only complaint is of the feet which are flat. Is married with one child. Does all her household duties without difficulty. Marked clubbing of fingers and toes and chronic swelling with infiltration of the skin and subcutaneous tissues of the legs below the knees. Chest examination completely negative. Radiographs show rough thickening of the lower parts of the radii and ulnae, tibiae and fibulae and some smooth hyperostosis of the lower thirds of the femora. Skull shows the vertical measurement reduced and the occipital projecting and pointed. Blood examination normal. Wassermann negative. Has eight brothers and two sisters, only one brother (Case 164) has a similar condition. Others normal except that whole family have multiple skin nodules (sebaceous melanomata). (By courtesy of Mr H. H. Langston 1940.)



Fig. 465

Case 163—Forearm showing irregular subperiosteal thickening of the lower third of both radius and ulna, that on the ulna being irregular.



Fig. 466

Case 163—Femur showing smooth thickening of the lower third of the shaft.





Fig. 467

Case 163—Legs showing the bilateral enlargement of both bones, with definite irregularity of the surfaces. The tibiae have no definite cortices.

CASE 164—IDIOPATHIC FAMILIAL HYPERTROPHIC OSTEOARTHROPATHY

(Figs. 468 to 470) I H male aged forty-seven Brother of case 163 History similar to that of his sister Clubbed fingers and enlarged wrists and lower part of legs for as long as he can remember Has led a normal active life Recently pain in left knee (arthritis) Ankles do not trouble him and are surprisingly free and painless Legs not tender Radiographs show changes almost identical with those of his sister in the bones above the wrists and ankles and some thickening of the femoral shafts Skull is of same shape as his sister's. In the tibia and fibula there is little sign of the cortices the bones being of uniform density Signs of osteoarthritis in left knee and tarsal joints patella very thick. Slight periosteal changes in lower part of one humerus the os calcis and some metacarpals Tufts of terminal phalanges are of unusual shape Chest examination completely negative Blood examination normal Wassermann negative (Under Mr H H Langston)



Fig. 468

Case 164—Skull showing curious shape similar to that of his sister Pituitary fossa appears to be roofed over this was not present in the sister's skull



FIG. 469

Case 164.—Legs showing the thickening of the bones, with some irregularity of the surface and loss of differentiation of cortex from medulla.



FIG. 470

Case 164.—Wrist and hand showing the peculiar hyperostoses of the radius and ulna and of the two inner metacarpal

CHAPTER 86

ERRORS OF THE HAEMOPOIETIC AND LYMPHATIC SYSTEMS

LEUKAEMIA

This condition is characterised by marked increase in the proportion of one or more types of leucocytes in the blood. It is associated in some cases with skeletal changes. The disease in children has been admirably reviewed by Whitby and Newns (1940) and the skeletal lesions by Silverman (1948) and Snapper (1949).

Of the various types of the disease lymphatic leukaemia accounts for 75 per cent. of the cases in children. The myeloid type is more frequently seen in adults. The monocytic type is rarely met with, particularly before the age of five years.

Hereditary and familial influences—In a few instances more than one member of a family have developed the disease.

Sex—Both sexes are affected, males rather more commonly, but Dale (1949), in seventy two cases in infants and children, found girls more affected among those under four years.

Age—It may occur at any age from a few weeks upward, being most frequent in the first four years of life. It is uncommon in adolescence; adults may be affected.

Etiology—The cause is still obscure, but there is a tendency towards regarding it as a neoplastic disease of the bone marrow (Whitby and Newns 1940).

Signs and symptoms—Early signs are pallor, asthenia and lassitude. The abdomen becomes distended with the spleen and liver enlarged. The glands in the neck, axillae and groins are swollen. There is slight irregular fever. Haemorrhages occur from the gums, nose, tonsil, bowel and urinary tract. The skin becomes mottled with petechiae. There may be retinal haemorrhages. Stomatitis may be troublesome. Pains in the limbs and tenderness of the bones occur. In the myelocytic type the spleen is particularly enlarged.

Blood examination reveals gross anaemia, both the red cells and the haemaglobin being much reduced. The platelets are at a very low level. The white cell count is often not much raised, particularly in the more acute cases, and not infrequently it is below normal temporarily. The count may, however, reach 200,000 and in the myelocytic type, unless a case is particularly acute, it may amount to 400,000. In the more common lymphocytic type the proportion of lymphocytes may be 75 to 90 per cent. Aleukaemic leukaemia is now regarded as a phase rather than a separate disease (Whitby and Newns 1940). In the diagnosis of this type sternal puncture is said to be particularly useful.

Radiological appearances—Reports of the frequency of radiographic changes in the bones in leukaemia are rather conflicting, but they appear to be more common in the lymphatic than the myeloid type. Bone lesions are more common in children than in adults, and in the subacute cases of both types, lymphatic and myeloid (Snapper 1949). Skeletal changes were found in fifty two of 103 leukaemic children studied by Silverman (1948). Three types of change occur—decalcification, osteosclerosis and subperiosteal shadows. Decalcification may be seen as longitudinal areas of rarefaction overlaid by delicate periosteal reaction, or as triangular areas of rarefaction in the shafts near the epiphysial lines—both these changes are regarded as characteristic by Geschickter and Copeland (1949)—or as a clear transverse band in the metaphysis similar to that seen in scurvy (Baty and Vogt 1935). This clear band may be separated from the epiphysial disc by a line or narrow band of increased density. Involvement of the adjacent cortex in the decalcification is often seen. The subperiosteal

shadows seen mostly towards the ends of the long bones but sometimes involving the whole of the shafts are striking in some cases. Silverman found these shadows in seventeen of fifty two children showing leukaemic skeletal lesions. The formation of a definite tumour is very uncommon the few reported cases have usually been of the myeloid type An appearance not unlike Ewing s tumour may be seen. Irregular increased density in the lower end of the femur in a case of lymphatic leukaemia was reported by Vaughan (1948) Occasionally there is more or less generalised osteoporosis the thin cortices may be overlaid by subperiosteal new bone (Gittins 1933)

The bones most commonly showing changes are the femur and humerus No part of the skeleton appears to be exempt though it is never universally involved. According to Windholz and Foster (1949) the leukaemic infiltration gives way to fibrosis and this is followed by osteosclerosis. Sclerosis, therefore occurs in the chronic cases such as may be met with in adults but this as already indicated is never generalised throughout the skeleton The skull shows diffuse granular mottling

Progress—Children die in a few weeks or months adults may live as long as two years.

Pathology—There is diffuse infiltration of the affected tissues with the particular type of cell predominating The bone marrow is usually red. Deposits in viscera are rarely seen in children. Enormous enlargement of the thymus has been seen in lymphatic leukaemia (Cockayne 1947)

Diagnosis—Biopsy may be necessary to exclude myelosclerosis in an adult Before it is discovered the skeletal changes are not confined to one bone osteomyelitis may be suspected. The smooth subperiosteal shadows seen in hypertrophic osteoarthropathy are more generalised than those seen in leukaemia

CHLOROMA

Chloroma is an extremely uncommon fatal condition met with usually in older children The features are myeloid leukaemic changes in the blood and the development of tumours which on section are green in colour The masses of various sizes may be either periosteal or endosteal and are seen in the orbit face skull and ribs they may also be found in the liver and kidneys The green colour fades on exposure to light The masses consist of non-granular cells indistinguishable from those of leukaemia and lympho sarcoma (Whitby and Newns 1949)

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CASE 165 ACUTE LYMPHATIC LEUKAEMIA

(Figs 471 to 473) B S male aged seven year Fall on back three months ago followed by pain in lumbar region Got well but pain recurred two month ago and general condition began to deteriorate with increasing pallor Lumbar kyphosis spine tender Irregular fever Spinal caries suspected and boy admitted to hospital Numerous palpable glands in neck axillae and groin Spleen only just palpable Blood red cells 1.2 million Haemoglobin 10 per cent White cell 4,200 Lymphocyte 70 per cent Lymphoblasts 1 per cent E.S.R 130 millimetres in one hour Radiographs showed the dorsal and lumbar vertebral bodies atrophic and shallow and the discs abnormally deep Pelvis and upper femora affected by somewhat irregular diffuse decalcification with subperiosteal shadows on the ilia and inner side of femoral shafts Ribs showed well marked subperiosteal shadows of even thickness Child died four days after admission No autopsy (Under Mr H H Langston)



Fig. 471
Case 165—Spine showing osteoporotic shallow vertebral bodies and increased thickness of the discs.

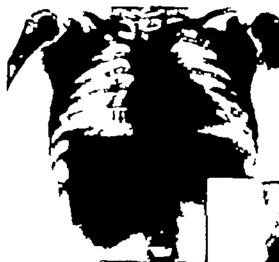


Fig. 472
Case 165—Thorax showing smooth subperiosteal shadows on many ribs



Fig. 473
Case 165—Pelvis and upper femora showing the coarse-grained decalcification of the bones—except the femoral heads—and subperiosteal shadows on the ilia and, to a slight extent on the femora

CASE 166—MYELOBLASTIC LEUKAEMIA

(Fig. 474.) M. M., male, aged four and a half years. Six months ago had slight generalised enlargement of lymph glands with normal blood count at that time. Left knee became swollen, with oedema in popliteal space. Was operated upon as acute osteomyelitis of femur. Had fleeting bone pains; acute rheumatism and Still's disease considered as possible diagnoses. Spleen was enlarged. White cells varied from sub-normal to 12 000, but were usually below normal. Left ankle swelled. Temperature 103 degrees. On admission bone marrow examination showed granulocytes 30 per cent. Lymphocytes 70 per cent., of which half resembled paramyeloblasts. Developed pain and tenderness of right wrist, knee and ankle. Liver and spleen enlarged. Blood: white cells 22 400, polymorphonuclears 22 per cent., lymphocytes 78 per cent. Radiographs showed extensive osteolytic changes in the long bones, particularly towards the ends of the shafts and in the epiphyses. No subperiosteal shadows. Under treatment with aminopterin his general condition was unchanged, but some sclerosis was noted in previously rarefied areas in upper end of one fibula. (Under Dr R. E. Bonham-Carter.)

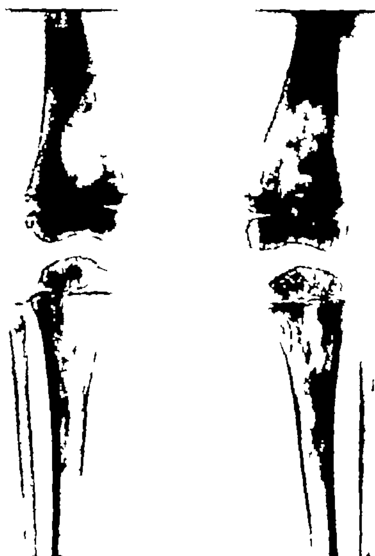


Fig. 474

Case 166—Legs showing changes, mostly osteolytic, towards the ends of the shafts of all the bones and in the epiphyses.

CASE 167—ALEUKAEMIC LEUKAEMIA

(Figs 475 to 478) A W female aged thirteen years Pain in legs for past nine months Seven months ago legs gave out Spinal lesion discovered six months ago Admitted for spinal caries and paraplegia Angular curvature in dorso-lumbar region Swelling of upper third of tibia and thickening of postero-internal aspect of lower third of left humerus Limited exten ion of elbow Voluntary movement of both legs poor Knee jerks exaggerated Ankle clonus present Plantar responses extensor Blood examination red cells 4 0 million Haemoglobin 88 per cent White cells 9 800 Polymorphonuclears 18 per cent Lymphocytes 10 per cent E.S R * millimetres in one hour (Later blood showed no material change White cells 7 400) Alkaline and acid phosphatase within normal limits Biopsy of right tibia Culture sterile Section ? leukaemia ? sarcoma Sternal puncture no suggestion of leukaemic change Radiographs showed irregular decalcification in the upper third of right tibia with erosion of the cortex of the lower half of left humerus and of the upper third of right humerus with the head of this bone almost detached by erosion There was a small cortical lesion on the inner side of the left humeral neck and collapse of D 10 vertebral body with some wedging of D 9 but without signs of a paravertebral abscess There was slight mottled decalcification of the ilia and the upper ends of the femora and changes in the middle third of the left tibia similar to those in the right Later emaciation increased There was weakness of the arms particularly the left Masses of glands developed in the axillae and in both supraclavicular regions particularly the left Reaction of the pupils to light and accommodation became very poor Nystagmus developed Died four months after admission Post mortem both kidneys and suprarenals were enlarged and filled with tumour Mass of glands at base of mesentery Collapsed vertebra was soft and replaced by * tumour Cause of death uraemia. Sections of glands liver etc showed typical leukaemic infiltration (Under the late Sir Henry Gauvain)



FIG 475

Case 167—Spine showing collapse of the tenth dorsal body with some wedging of the ninth



FIG 476

Case 167—Right shoulder show ng the changes in the upper third of the humeral shaft and partial separation of the head



FIG. 477

Case 167—Right leg showing irregular decalcification in the upper third of the tibia.

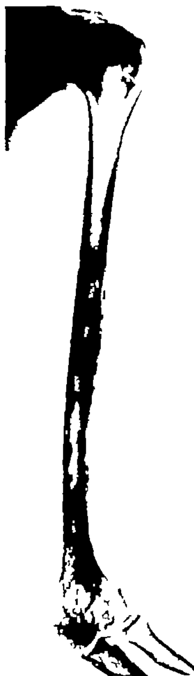


FIG. 478

Case 167—Left arm showing irregular decalcification of the humeral shaft. Note the small lesion on the inner side of the neck of this bone.

CHAPTER 87

HODGKIN'S DISEASE

Lymphadenoma

This is a disease of the haemopoietic system characterised by enlargement of the spleen and lymphatic glands and the development of changes in the bones. Lymphosarcoma and leukaemia are regarded as closely allied to it. Whitby and Newns (1943) have published a useful up-to-date account of the subject.

Hereditary and familial influences play no part in the incidence.

Sex—Males are affected twice as frequently as females.

Age—It occurs at all ages but is uncommon in childhood and is most frequently seen in young adults.

Etiology—The cause is unknown. By some it is regarded as lymphoblastoma which may develop either into lymphosarcoma or lymphatic leukaemia (Whitby and Newns 1943).

Signs and symptoms—There is discrete soft enlargement of glands, commonly in the neck, splenomegaly, fever, anaemia and cachexia. Fever may be continuous, intermittent or remittent (Thursfield 1931). The glandular swellings which increase and spread are painless but there may be pain due to osseous lesions in the legs, lumbar region or sternum. Skin lesions occur in about a third of the cases; in some there is pigmentation. A fluctuating swelling on the head produced by an unusually large skull lesion was reported by Moir and Brockis (1949). Radiologically demonstrable osseous lesions were found in 1? per cent of cases by Craver and Copeland (1934) but examination of the skeleton after death suggests ?0 per cent is a more accurate figure.

Blood examination reveals nothing of importance. The alkaline phosphatase is raised; eosinophilia occurs in 15 per cent.

Radiographic appearances—Most lesions are osteolytic but some are osteoplastic and others a mixture of the two. There may be cortical thickening or the cortex may be eroded either from within or from without with periosteal reaction visible only at the extremities of the growth. Sclerosis similar to that seen in Garré's osteitis has been reported (Schenck 1937). We have seen one case in which the periosteal reaction was spicular. The bones most frequently affected are the vertebrae, sternum, pelvis, femora, ribs, skull, humeri, scapulae and clavicles. In the long bones the lesions usually occur near the proximal ends but the whole of a bone may become involved. In the skull the lesions are osteolytic, multiple and spotty, not unlike those seen in myelomatosis though less sharply cut. A vertebral body may be sclerosed with or without collapse; occasionally several bodies, usually of consecutive vertebrae, are affected (Dresser and Spencer 1936, Snapper 1940). The discs are not involved. A paravertebral shadow similar to that seen in spinal caries may be present (Scott 1948).

Progress—The degree of malignancy varies but it is always fatal eventually, usually in one to three years from the onset.

Complications—Crush fractures of a vertebral body and fracture of one or more ribs may occur. Paraplegia may result from pressure when vertebral bodies are infiltrated (Cade 1940). Weber (1909) reported a case of Hodgkin's disease with clubbing of the fingers and changes typical of hypertrophic osteoarthropathy in all the long bones of the extremities.

Pathology—Recently formed nodules are pale pink on section and the older ones white. They may be found in any and every organ in addition to the glands and the spleen, in which

] <r te ir ular masses are seen The lesions are more of the nature of a granuloma than a { la m. Microscopic examination reveals proliferation of lymphoid cells with the appearance r re } e cells with elongated vesicular nuclei, Reed-Sternberg giant cells and eosinophil L t n ecrosis and fibrosis are seen (Whitby and Newns 1949)

B n nvolvement in *lymphosarcoma* is distinctly less common than in lymphadenoma pl i i less affected and the liver much more so than in Hodgkin s disease ph sar oma usually occurs after the twentieth year The distribution of the bone i is much the same as in Hodgkin s disease the spine pelvis and skull being most quently affected The lesions may be predominantly osteoplastic or osteolytic. In the kull there is the same tendency for the appearance of multiple small clear holes as m my lomatous (Geschickter and Copeland 1949)

Diagnosis—It may be impossible to diagnose Hodgkin s disease or lymphosarcoma from rcinomatosis without biopsy of a gland. Lesions below the knees and elbows are not seen in Hodgkin s disease but they may be though only occasionally in carcinomatosis (Snapper 1949) In the early stages diagnosis from tubercular glands which are less likely to be discrete may also be impossible without removal of a gland. In lymphatic leukaemia there is a ndency to haemorrhages and characteristic changes are present in the blood.

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CASE 168—HODGKIN'S DISEASE

(Fig 479) J T female aged thirty two years Diagnosed when twenty three years old by biopsy of a supraclavicular gland Treated by X ray therapy Recently developed polyneuritis with variable weakness and loss of reflexes secondary to lung infection due to bronchial obstruction Moderate ataxia Cerebro-spinal fluid 100 lymphocytes per cubic millimetre General enlargement of lymph glands Radiographs showed mixed sclerosis and "cystic" lesions in left ilium and a rounded shadow at back of right lower lobe pressing on bronchus verified by bronchoscopy Blood marked anaemia. White cells 14 000 Neutrophils 84 per cent E.S.R. 30 millimetres in one hour Spleen and liver enlarged. Febrile for several weeks. Translucent area ? deposit in mid-shaft of left tibia Considered to have root pains probably due to Hodgkin deposits not detected by X-rays (Under Professor B W Windeyer)



Fig 479

Case 168—Pelvis showing lymphadenomatous deposit in the left ilium with considerable sclerosis in addition to the osteolytic lesions

CASE 169—HODGKIN'S DISEASE

(Fig 480) J R female aged thirty five years Complained of lump in left side of neck for six months night sweats and loss of weight Lymph glands in neck enlarged Radiographs showed mediastinal glands enlarged. Biopsy of gland Hodgkin's disease Treated by X ray therapy Blood nothing abnormal Later white cells 12 600 to 1 800 and anaemia. Radiographs showed infiltration of one lumbar body (Under Professor B W Windeyer)



Fig. 480

Case 169—Spine showing lymphadenomatous deposit in second lumbar body with erosion of the anterior surface.

CASE 170—HODGKIN'S DISEASE

(Fig 481) G C female aged twenty-seven years Complained of lumps in neck for past four months Discrete glands in both posterior triangles. Biopsy of gland Hodgkin's disease Blood white cells 12 000 polymorphonuclears 80 per cent Treated with radium and later with several courses of X-ray therapy Radiographs showed opacity in superior mediastinum. Four years after diagnosis was made developed swelling over left second rib which increased in size later and large gland appeared in left axilla and later a large mass in right axilla Twelve years after onset she lost weight and died (Under Professor W B Windeyer)



Fig. 481
Case 170—Right chest showing pathological fractures through the fifth and sixth ribs, infiltrated with lymphadenomatous deposits. The seventh rib is also affected.



Fig 482
Case 171—Skull showing lymphosarcomatous infiltration closely resembling myelomatosis

CASE 171—LYMPHOSARCOMA

(Fig 482.) I S female aged twenty two years. Complained of palpitations breathlessness vomiting loss of energy and pains in chest. Tender over sternum in lumbar region and on ribs. Spleen not enlarged. Severe anaemia. Blood red cells 2 10 million Haemoglobin 48 per cent White cells 5 500 picture of leuco erythroblastic anaemia Urine no Bence-Jones protein Radiographs showed multiple clear lesions — closely simulating myelomatosis—in skull ribs pelvis left humerus femur and tibia (right arm and leg not examined) Died about eighteen months after the onset. Post mortem investigations showed lymphosarcomatous lesions (Under Dr A Gilpin)

CHAPTER 58

MYELOSCLEROSIS. OSTEOSCLEROTIC ANAEMIA

ALEUKAEMIC MEGAKARYOCYTIC MYELOSIS

This is a very uncommon condition allied to the leukaemias in which changes in the blood are associated with increased density of the skeleton.

Adults are most frequently affected, only a few cases in childhood and adolescence having been reported, and some of these appear to be questionable. It is seen in both sexes. The cause is unknown. The clinical picture consists of severe and progressive anaemia. Slight glandular swelling and marked enlargement of the spleen. Blood examination reveals changes said to be similar to both myeloid leukaemia and leuco-erythroblastic anaemia. The only constant change is reduction in the haemoglobin which may be at a very low figure. Sternal puncture is apt to be unproductive as the marrow is fibrotic or partially ossified; biopsy is often necessary to distinguish the affection from leukaemia. There are no symptoms directing attention to the bones, the changes in which are revealed only by routine radiographic examination. There is a varying degree of widespread osteosclerosis; the medullary cavities of the long bones, particularly the femora, are reduced in size by thickening of the cortices on their internal aspects. Irregular sclerosis, leaving multiple less dense areas, was seen in a case with leuco-erythroblastic anaemia and fibrosis of the marrow reported by Ferriman (1947). The essential pathological change in the bones is fibrosis, followed by osteosclerosis. Short reviews of value are those by Landoff (1944) and Vaughan (1948).

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ERYTHROBLASTIC ANAEMIA OF COOLEY

Mediterranean Anaemia

This condition is almost exclusively confined to young children in Mediterranean countries with a few Chinese, and therefore calls for only the briefest consideration here. There is general osteoporosis combined with curious thickening of the skull, particularly the frontal region. The outer table shows vertical striation, a lateral skiagraph being characteristic and diagnostic. Caffey (1945) reported a girl of four years with curious honeycomb changes in the metacarpals and phalanges.

Sickle Cell Anaemia occurs in negroes and is said to be similar to Cooley's anaemia, but the bone changes are much less marked.

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CAFFEY, J. (1945). Paediatric X-ray Diagnosis, p. 730. Chicago: Year Book Publishers.

CASE 172—MYELOSCLEROSIS

(Figs. 483 and 484.) H. S. male aged forty-six years. Abdomen swollen for last ten years. Spleen enlarged and gradually increasing in size. Short of breath. Ankles swollen. Anaemia marked. Sternal puncture inconclusive. Biopsy of iliac marrow showed some fibrosis macronormoblasts metamyelocytes and granulocytes. Splenectomy performed, spleen said to be typical of myelosclerosis. Examination later showed abdomen still swollen, liver enlarged. Oedema of ankles. Blood haemoglobin 40 per cent. White cells 22 000. Neutrophils 80 per cent. Nucleated red cells 8 800 per cubic millimetre. Red cells exhibit anisocytosis, central pallor and polychromasia. Among white cells some metamyelocytes and an occasional myelocyte. Radiographs showed generalised increased density of the skeleton with the exception of the skull and hands. Given blood transfusion. Later great difficulty in obtaining marrow by puncture. Blood showed twenty three nucleated red cells to every 100 white cells. (Under Dr J. L. Livingstone.)



Fig. 483

Case 172—Arm and forearm showing increased density of the bones and loss of contrast between cortex and medulla. The distribution of the density in the ulna is curious.

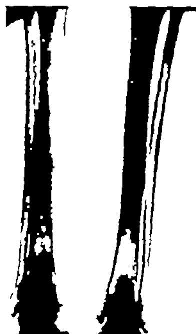


Fig. 484

Case 172—Legs showing increased density of the tibiae less marked the fibulae with little indication of the tibial cortices.

CHAPTER 57

MULTIPLE ANGIOMATA OF BONE

The classification of angiomatous tumours of bone appears to be a matter on which there is considerable difference of opinion, particularly with regard to the multiple tumours. Solitary angiomata are relatively common, e.g. in a vertebral body, and can often be diagnosed without difficulty; it is the cases with multiple lesions we are concerned with here, and these are very uncommon. Apparently both benign and malignant angiomata may occur as multiple tumours in the skeleton. Both types seem to produce a soap-bubble appearance. A remarkable case of generalised angiomatosis was published by Parsons and Ellis (1940) who discuss the subject fully. A girl of fourteen with an enlarged spleen was thought to be a case of Gaucher's disease until, after death from broncho-pneumonia, autopsy revealed cystic cavernous angiomata in the spleen, liver, lung, mediastinum, pleura, kidneys, thymus glands and most of the bones. The angiomata were apparently benign; the case was regarded by the authors as a form of reticulo-endotheliosis. They call attention to a closely similar case reported by Shennan (1914). A remarkable case of *skeletal haemangio-endothelioma* is reported by Hauser and Constant (1948); the upper ends of both femora, and later the pelvis and sacrum, developed enormous masses of "cysts", which apparently developed by direct spread from only two primary foci. The sufferer, a woman of forty years, was still alive seven years after a fracture revealed early changes at the upper end of one femur. We have seen cystic lesions in several bones of a man's foot which proved to be an angio-endothelioma. Direct spread from a single focus to all of the affected bones appeared to be improbable in this case. Thomas (194[illegible]) reported a case of malignant angioma in which the entire skeleton appeared to have been affected primarily. We have seen a young woman with atypical multiple small lesions in the radius and ulna associated with a diffuse naevoid condition of the index and middle fingers.

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SHENNAN, T. (1914). Journal of Pathology and Bacteriology, 19, 139.
THOMAS, A. (194[illegible]). Surgery, Gynecology and Obstetrics, 74, 777.

CASE 173—ANGIO-ENDOTHELIOMA

(Figs. 485 and 486.) Sergeant B, male, aged thirty-five years. Right foot swollen two years. Reported sick only six months ago with some discomfort in foot. Ankle and proximal part of foot swollen and definitely hot on inner side. Skin dusky red and mottled. Some limitation of movement of foot and ankle. No enlarged glands. Blood: white cells 11,800. Polymorphonuclears 60 per cent. Radiographs showed soap-bubble type of cystic change in most of the tarsal bones, the base of the fifth metatarsal, the anterior part of the lower extremity of the tibia, and possibly in the tip of the external malleolus. The external cuneiform and the cuboid are apparently free from growth. If this is correct the lesion in the fifth metatarsal must be a separate tumour and not the result of direct spread from another affected bone. Biopsy: angio-endothelioma. Treated by deep X-ray therapy and eventually amputation. (Under the late Major-General J. W. West.)

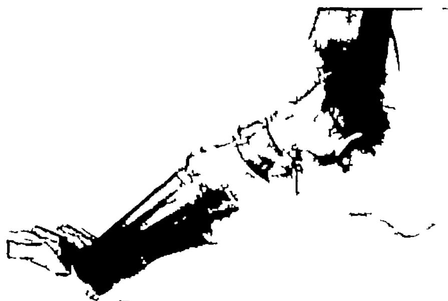


Fig. 485

Case 173—Lateral view showing the cystic changes in most of the tarsal bones and an apparently isolated tumour in the fifth metatarsal. The erosion of the tibia is well shown.

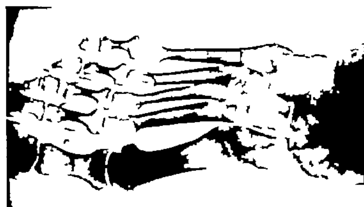


Fig. 486

Case 173—Antero-posterior view of the foot showing the growth in the tarsal bones with the exception of the cuboid and outer cuneiform. Possibly the fifth is not the only metatarsal involved in the growth.

CHAPTER 60

SKELETAL METASTASES

It is said that of all fatal cases of malignant disease 20 to 30 per cent have metastases in bone and almost invariably the metastases are multiple (Willis 1934). If carcinomas of the breast, kidney, prostate and bronchus only are considered the percentage with osseous metastases rises to 50 and in 25 per cent the metastases are clinically manifest (Geschickter and Copeland 1949 (*a*)). Most cases showing skeletal metastases are over thirty five years of age, usually in the age group of forty to sixty (Roberts 1939). The age incidence varies with the site of the primary growth. Both sexes are necessarily affected. The usual method of production of a metastasis in bone is said to be by retrograde extension through valveless veins in the intercostal and vertebral systems (Batson 1940, Geschickter and Copeland 1949 (*a*)), but the spread of a prostatic carcinoma to the pelvis, sacrum and lumbar spine may be via lymphatics. The primary lesions most frequently responsible for metastases in bone are carcinoma of the breast, prostate and thyroid and hypernephroma. The bones affected by metastases of all kinds, in order of frequency, are the spine, pelvis, ribs, skull, femur and humerus. Bones distal to the elbow and knee are rarely affected. The local signs most frequently attracting attention to a metastasis are pain and spontaneous fracture. Pain may be present for long before there is radiographic evidence of the cause, but pain is by no means always present, even when the bone is about to fracture or collapse. When the spine is invaded root pain may be complained of. It is well known that a long period, even several years, may elapse from discovery of a primary growth before the appearance of one or more metastases. On the other hand a metastasis is not infrequently the first sign of danger, there being nothing to suggest the presence of a primary growth anywhere in the body, sometimes even when its locality, e.g. a hypernephroma, has been revealed by histological examination of a metastasis. Occasionally a pathological fracture due to a metastasis may unite with or without the help of radiotherapy. Pulsation may be felt and a bruit heard in a metastasis, but only in cases of thyroid and renal growths (Willis 1934). There may be haemo-erythroblastosis when the marrow is extensively invaded. The alkaline phosphatase in the blood is often raised; in prostatic metastases the acid phosphatase is markedly increased. When the destruction of bone by osteolytic metastases is particularly rapid hypercalcaemia may be present (Coley and Higinbotham 1949). The blood sedimentation rate may also be abnormally high. Bence Jones protein may be present occasionally in the urine in carcinomatosis (Geschickter and Copeland 1949 (*b*)). The type of lesion seen in a skeletal metastasis varies with the primary growth. It may be either endosteal or periosteal or both and it may spread from the bone into the soft tissues. The changes may be osteolytic or osteoplastic or a combination of the two. Early metastases are more osteoplastic than later. Osteoplastic lesions spread more slowly than osteolytic and are more likely to be confined to the bone; a case may live three or four years after the discovery of several osteoplastic metastases. Towards the end no new bone is formed, any new lesions that develop being osteolytic (Hodges *et al.* 1941). Fractures and crushed vertebral bodies are more common in osteolytic lesions.

There may be extensive carcinomatous infiltration of the bones with no definite radiographic changes. Occasionally onion skin laminae form on the surface and even sunray spicules vertical to the surface may occur in a carcinomatous metastasis, e.g. in a secondary neuroblastoma; such a growth may be readily mistaken for a sarcoma (Willis 1948). We have seen this appearance in a prostatic metastasis. A useful guide to the type of skeletal lesion

to be expected in each of the four carcinomas that most frequently metastasize to bone was published by Hellner (1934) his list is the following 1) Osteolytic without bone reaction (breast or hypernephroma) 2) Cyst like with formation of a surrounding shell (hypernephroma or thyroid) 3) Piebald or Pagetoid (breast or prostate) 4) Purely osteoplastic (prostate) The denser sclerotic type of metastasis is more likely to arise from a slow growing carcinoma e.g prostate scirrhus of breast and stomach (Baker 1930) Platt (1933) would add the bronchus to this list

In carcinoma of the *breast* most metastases are osteolytic and the lesions endosteal the cortex being invaded from within The cortex may be thickened above or below the lesion in a long bone (Geschickter and Copeland 1949 (*c*)) When the primary growth is of the scirrhus type a metastasis is more likely to occur and to be osteoplastic. A case with several vertebral bodies showing increased density such as may be seen in Paget s disease is published by Hodges *et al* (1941) Occasionally multiple small osteolytic lesions are present and the appearance may closely resemble myelomatosis as in the case with the skull and humerus affected published by Geschickter and Copeland (1949 (*c*)) The spine pelvis and femur are most commonly affected, with the skull ribs and humerus less often the seat of a metastasis. In one case we found extensive metastatic involvement of the pelvis with central dislocation of one femoral head, eleven years after removal of a cancerous breast eighteen months elapsed before the patient succumbed. Examination post-mortem of cases dying of cancer of the breast showed 92 per cent had skeletal metastases (Hodges *et al* 1941)

In *prostatic carcinoma* metastases which are at least partly osteoplastic are usually regarded as typical. My friend Mr John Everidge—a man with an enormous experience of these cases—tells me he considers the tendency to osteoplastic changes in prostatic metastases has been much exaggerated. Some patches of increased density certainly appear to be common far commoner than in any other metastases and in a male of suitable age they should be regarded as distinctly suggestive Mr Everidge showed me a pathological fracture of the femur due to a prostatic metastasis which was entirely osteolytic. 60 per cent of the cases examined after death show metastases in the bones The pelvis lumbar spine and upper femora are the sites of election and are rarely free if the skeleton is affected. The changes are often patchy there being clear spots as well as dense producing a piebald appearance In other cases the density is more uniform particularly in the vertebrae The affected bones may or may not be thickened. The appearance produced by osteoplastic prostatic metastases has been described as secondary marble bones (Weber 1933) a term which seems particularly appropriate for the case of generalised myelofibrosis with progressive eburnation due to skeletal invasion with prostatic carcinoma reported by Bernack and Feinstein (1946) A prostatic metastasis in a humeral shaft appeared to be curiously spicular in a radiograph published by Coley and Higinbotham (1940) It is said the bone may be so dense it can be sawn only with difficulty The prostate itself may or may not show clinical signs of neoplastic invasion. The amount of acid phosphatase in the plasma is a valuable diagnostic sign in doubtful cases. Anything below three units per 100 cubic centimetres excludes bone invasion from a prostatic growth and anything over five units almost certainly indicates it (Lancet 1943) Ten units or more may be regarded as absolutely diagnostic (Huggins and Hodges 1941)

Metastases from the thyroid are usually distinctly cystic in appearance and are not unlike an osteoclastoma except for their position in the affected bone Carcinoma of the thyroid is only surpassed by mammary and prostatic growths in the frequency with which it metastasizes to bone The upper half of the body is favoured the sites of metastases in order of frequency being the skull sternum ribs humerus femur and pelvis Pulsation may be felt in a metastasis, particularly when this has occurred many years perhaps over twenty after operation on a thyroid which may have been regarded as the seat of simple hyperplasia or

at most of a benign tumour In some cases microscopic examination of a solitary metastasis may supply the first and even the only indication that the thyroid is responsible examination of that gland showing either what appears to be an innocent enlargement or no abnormality whatsoever In some of the cases more than one m ta ta is has been present The appearance as regards innocence or malignancy of the section of the thyroid and that of the metastasis by no means always agree and may differ con iderably (Joll 1923) Apparently the degree of malignancy of growths of the thyroid varies enormou ly and it is the type of low malignancy which gives rise to osseous metastases (Connell 1930) Erosion of the cortex and invasion of the soft tissues is more often met with in thyroid than in other metastases

The great majority of *hypernephromas* are carcinomas of renal epithelium and do not arise in misplaced adrenal tissue (Geschickter and Copeland 1940 (*d*)) About one third of the cases meta tasize to bone The secondary growths are definitely osteolytic and cystic in appearance and are rather inclined to be solitary occasionally pulsation can be felt The spine pelvis femur humerus skull sternum and ribs are the more common sites

Carcinoma of a *bronchus* may give rise to one or more osteolytic metastases in bone though less commonly than those already referred to According to Coley and Higinbotham (1940) the location of the metastases is unusual the humerus femur upper tibia and clavicle on the side opposite to the affected lung being the more common sites We have seen a femur fractured through a metastasis from an unsuspected bronchial carcinoma. Cosin (1935) reported a proved case with metastases in many bones particularly in the skull where many punched-out clear lesions gave the appearance typical of myelomatosis

The diagnosis when there has been no sign of a primary growth may be extremely difficult and involves consideration of many different types of tumours and diseases of bone If generalised decalcification is marked the possibility of hyperparathyroidism as the cause may arise Secondary hyperparathyroidism may however develop in carcinomatosis in such cases there is usually hypertrophy of all four glands and only exceptionally an adenoma Snapper (1949) quotes a case of special difficulty one of carcinomatosis with many osseous metastases and in which the serum calcium rose to 17 milligrams per 100 cubic centimetres, the phosphorus being normal in amount and the alkaline phosphatase raised while the excretion of calcium was much increased. No parathyroid tumour was discovered after death. Some cases of diffuse carcinomatosis live surprisingly long one such case lived for seven years (Hunter 1938) In the patchy type of atrophy most frequently met with we believe after a fracture which is being treated by complete immobilisation the appearance may be very suggestive of carcinomatous infiltration The presence of metastases in the lungs makes myelomatosis an almost impossible diagnosis. Large spherical metastases few in number in the lungs are in favour of sarcoma rather than carcinoma (Hodges *et al* 1941)

In *sarcoma of bone* skeletal metastases are decidedly uncommon but do occur occasionally The same is even more true when the primary growth affects soft tissues (Willis 1934) Geschickter and Copeland (1949 (*e*)) found in thirty-seven cases of Ewing s tumour which had metastases in the lungs or bones that five had multiple bone lesions. Several bones may be affected at the same time. In the later stages metastases favour glands and the skeleton rather than thoracic and abdominal viscera (Platt 1933) In Paget s disease multiple sarcomatous tumours may appear in the skeleton as a rule the tumours occur only in bones showing Paget changes (Davie and Cooke 1937) In a case with both sarcoma and Paget s disease affecting the skull, a metastasis in a lung was found to contain bone by Dr L. M Hawksley (1934) We know of a case of lymphosarcoma with most of the skeleton including the skull showing multiple small clear lesions the appearance being typical of myelomatosis.

It does not appear to be generally known that a sarcoma of bone may give rise to hypertrophic osteoarthropathy with typical and widespread changes in the long bones.

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CASE 174—METASTASES FROM CARCINOMA OF BREAST

(Figs. 48 to 489) A. F. femal aged forty nine years. Radical amputation of right br a t in February 1929 for spheroidal celled carcinoma ix month after growth had been discovered. In August 1930 developed rheumati m in right shoulder which teadily increased in severity. Radiograph first taken one year later. These howed meta tases in right clavicle humerus and scapula the pelvis and upper part of both femora pine and several rib on right side. Later radiographs suggested diffuse carcinomatosis of whole keleton. Bl od examination howed severe apla tic anaemia and relative lymphocytosis. Died in Oct ber 1931. Post mortem complete absence of red marrow. Diagnosi confirmed.



Fig. 487

Case 174—Right shoulder showing osteol tic lesion in the outer end of the la icle the h merus and the scapula adjacent to the glenoid.



Fig. 488

Case 174—Pelvis and upper parts f femora showing widespread metastatic deposits, mostly osteolytic but partly osteoplastic.



Fig. 489

Case 174—Chest showing multiple small metastases in the ribs, mostly those on the right side and on the right scapula close to the axillary border



CASE 175—METASTASES FROM CARCINOMA OF THE BREAST

(Fig 490) Mrs McN., aged thirty-nine years. Complained of pain in left leg for past three months. Radiograph showed metastasis in upper end of left femur. Two years ago had breast removed for scirrhus carcinoma with glands extensively involved. Two days ago leg gave way. Examination showed many enlarged glands in neck. Later masses developed in abdomen and chest. Died about twelve months after discovery of femoral metastasis. (Under Sir John Weir)

Fig. 490

Case 175—Left hip showing purely osteolytic metastases involving the upper end of the femur and another eroding the outer cortex of the shaft. (Film taken ten months after discovery of the metastasis.)

CASE 176—METASTASES FROM PROSTATIC CARCINOMA

(Fig. 491.) A. C. aged seventy-five years. Complained of difficulty in micturition for three years, much worse during past month. Hesitancy marked. Dribbling thin stream. Haematuria occasionally for past nine months. No clots. Sciatica in left leg for three months. Is losing weight. Bladder distended. Rectal examination: carcinoma of prostate. Radiographs showed multiple osteolytic metastases with some osteoplastic mottling in left side of pelvis with central displacement of femoral head. Lumbar spine also shows some changes. Suprapubic cystostomy performed. (Under Mr J. C. Yates-Bell.)



Fig. 491

Case 176—Pelvis showing metastases, mostly osteolytic, involving particularly the left ilium and ischium, with destruction of the acetabulum and central displacement of the femur.

CASE 177—METASTASES FROM PROSTATIC CARCINOMA

(*Figs. 492 to 496.*) *H. D.* aged sixty-seven years. Troubled with low back pain for years, worse during last few months. Pain now radiates down left thigh and leg to ankle. On examination the lower part of the left leg puffy and varicose veins prominent. The left buttock—the seat of much pain—and the lower end of the left tibia were markedly tender. Movements of trunk very restricted. No neurological signs in left leg. Radiographs showed marked increased density with distortion of the surface in left side of pelvis and adjacent part of sacrum. Some changes also in the head and neck of left femur, a small dense area in the anterior part of right ilium and increased density about the right sacro-iliac joint. The shaft of the left tibia showed increased density and there were two dense patches in the left os calcis. Prostate felt normal. No sign of primary neoplasm discovered anywhere in body. Blood examination: acid phosphatase 10 units per 100 cubic centimetres (King method).

Lower part of spine and left hip became extremely stiff Four months later there was some extension of the lesions in the pelvis with distortion of the surface on the left side Most of the shaft of left tibia was now involved and a dense spot was seen in the outer tuberosity and another near the tibial spine A large dense area was seen in the head of the right tibia. He was treated by stilboestrol with dramatic success. Sixteen months later patient is in good general health and able to work on his farm. Is taking 10 milligrams of stilboestrol daily No serious pain anywhere now Prostate still shows no abnormality slight frequency of micturition at night Puffiness of left lower leg and the tenderness are much diminished Movements of left hip considerably restricted but no longer painful. Recent radiographs show the changes in the left side of the pelvis are of more uniform density and the surface more clearly defined no obvious extension of the growth. Lesions in the head of the left tibia less dense but slightly larger Some diffusion of the growth in the os calcis and possible extension to other tarsal bones. Extension of the dense changes in the left tibial shaft is obvious the posterior surface is now distorted. (Under Mr G T Partridge)



FIG. 492

Case 177—Pelvis and hips (December 1948) showing the extent of the metastases. Note the patches of increased density in the anterior part of the right ilium and about the right sacro-iliac joint and changes in the neck of the left femur



FIG. 493
Case 197—Legs (December 1948 show g dense metastases in the heads of both t biae nd changes in the shaft of the left tibia.



FIG. 494
Case 177—Left k ee (April 1950) how ing the two meta tases ha xtended little but are less dense



FIG. 495
Case 177—Left leg (August 1948) showing increased density i the tibial shaft with slight changes on the surface and two dense areas in the os calcis.



FIG. 496
Case 177—Left leg (January 1950) showing the striking in crease in the changes in the tibia and the subperiosteal new bone particularly on the posterior surface Note the dense shadows in the os calcis are more diffuse and appear to have spread into th cuboid and navicular

CASE 178—METASTASES FROM CARCINOMA OF THYROID

(Figs. 497 and 498) F C. female aged forty-nine years. In 1030 noticed tightness of throat and difficulty in swallowing over a period of five months Small hard mass found in right lobe of thyroid apparently an adenoma. Partial thyroidectomy performed. November 1944 fell and fractured shaft of left humerus. Treated as traumatic fracture February 1945 refractured left humerus at same site Radiographs then suggested osteoclastoma at site of fracture Given a course of deep radiotherapy On admission in January 1040 excision of tumour in humerus and insertion of fibular graft and cancellous chips from ilium. Graft unsuccessful Radiograph showed possible metastasis in great trochanter of left femur Tumour in great trochanter excised. Microscopic section showed glandular tissue from thyroid Hard adenoma found in right side of thyroid isthmus tumour size of hen's egg removed. Section showed adenomatosis of the colloid type September 1047 general condition excellent. No sign of recurrence in great trochanter film shows only sclerosis. Humerus still ununited. Metastasis, of uniform density and not cystic, now present in upper end of humerus. Removal of this is proposed. (Under Mr T T Stamm)



FIG 497
Case 178—Left humerus showing cystic thyroid metastasis the shaft, with pathological fracture



FIG. 498
Case 178—Left femur showing osteolytic thyroid metastasis in great trochanter

CASE 179—METASTASIS FROM CARCINOMA OF THYROID

(Fig. 499.) S. R. female, aged fifty-four years (194?). In 1914 first noticed swelling of thyroid. In 19?0 noticed tightness of throat and difficulty in swallowing. Small hard mass found in right lobe of thyroid. In 19?? thyroidectomy performed. In 1941 fell and fractured right femur. Union very slow, so after some months a biopsy performed. Section showed secondary thyroid growth.

Fracture eventually united without X-ray therapy and patient discharged with caliper. Walking well without pain for five months when fracture recurred. No signs of union appeared and tumour increased in size. No other metastases discovered, so limb was disarticulated at hip joint (March 1943). Fourteen months later no sign of further growth. (Under Mr F. J. Radley Smith.)



Fig. 499

Case 179—Shows partial union three months after pathological fracture through extensive metastasis in femur.

CASE 180—METASTASIS FROM HYPERNEPHROMA

(Fig. 500.) A. P. S. male, aged fifty-five years. Complained of left "sciatica" during past eighteen months. Pain is chiefly in buttock, spreading round to the groin. Worse on sitting. No other symptoms. Healthy looking man. Hard pulsating swelling size of half a grapefruit felt in left buttock. Hamstrings flaccid but no paralysis in leg. Some 10 degrees of fixed flexion of hip. Flexion full. Abduction and rotation limited. Straight knee flexion of hip produced severe pain in hamstrings. Rectal examination negative. Urine normal. Radiographs showed complete disappearance of the left ischium and an osteolytic lesion invading the ilium in the floor of the acetabulum and also the femoral head. A thin irregular line of calcification indicates what is apparently the limit of a tumour projecting into the pelvic cavity. Operation revealed a tumour with a fibrous slightly gritty shell. Incision opened a cavity occupying about a fifth of the tumour and lined with brown granulomatous growth; fluid doubtful, possibly only blood. Bled freely so cavity plugged. Pathologist's report: hypernephroma. Nothing abnormal to be felt in abdomen. Five months later he was sinking rapidly.



Fig. 500

Case 180—Left side of pelvis showing complete replacement of the ischium and invasion of the acetabular portion of the ilium and the femoral head by an osteolytic growth. Note the calcified shell of the tumour in the pelvic cavity.

CHAPTER 61

MULTIPLE MYELOMA

MYELOMATOSIS KAHLER S DISEASE

This is a fatal neoplastic disease characterised by diffuse infiltration of the marrow with myeloid cell and widespread formation of multiple myeloid tumours both in the skeletal and in various non-osseous tissues and it is associated in the majority of cases with Bence Jones protein in the urine. This protein was demonstrated by Bence-Jones as early as 1848 while multiple myeloid tumours were described by Rustizky in 1873 the association of the two was first noted by Kahler (1889) so myelomatosis is often referred to as Kahler's disease Valuable reviews have been published by the Lancet (1948) and by Snapper (1949)

Hereditary and familial influences play no part in the incidence

Sex—Males are affected at least twice as frequently as females. Ghormley *et al* (1939) found sixty-three males and twenty three females among their cases.

Age—It occurs most frequently in the age period forty to sixty years Though myelomatosis has been reported in adolescents and even in children the diagnosis in these cases does not appear to be generally accepted.

Distribution—Geschickter and Copeland (1928) reviewed 425 cases and found skeletal lesions often confined to the spine and ribs. Other fairly frequent sites are the skull and the femora and in the later stages the clavicles and humeri The mandible has been the seat of a primary lesion (Wolff and Nolan 1944) Of the non-osseous tissues the spleen glands and liver are most commonly affected lesions have also been found in the thyroid, kidneys pancreas viscera and heart The lungs usually escape multiple bone lesions with the lungs entirely free from tumours is regarded as typical of myelomatosis by Ogilvie (1939) In addition to the tumours there is diffuse infiltration of the marrow

Signs and symptoms—Undue fatigue refractory anaemia and cachexia are usually present sooner or later As a rule the patient complains of bone pains particularly in the lower back and thorax the pains may shift from place to place and may be intermittent A haemorrhagic tendency with epistaxis may develop There may be pyrexia In some a palpable tumour is present in others a pathological fracture e g of a rib is the first sign but this is exceptional. *Though involvement of the skull is common there is no sign of abnormal intracranial pressure* and the cranial nerves are not affected Tumours may be visible on the scalp and occasionally a hole in the skull may be felt Sometimes spinal root pains are complained of and compression of the cord may follow collapse of a vertebral body Sternal or iliac puncture seldom fails to show plasma cells of normal and abnormal types in large numbers but very occasionally the puncture gives a negative result in a case otherwise proved to be myelomatosis.

Blood examination—Anaemia is invariably present As a rule the white cell count is normal but very occasionally they are increased in number with various immature and abnormal cells the picture of plasma cell leukaemia developing towards the end (Snapper 1949) Lymphocytosis and eosinophilia seldom occur Myeloma cells may be found in the blood. The blood platelet are reduced The E S R. is increased. In more than half the cases the globulin is increased The serum calcium may be increased in amount even to as high as 20 milligrams per 100 cubic centimetres myelomatosis and hyperparathyroidism are the only conditions showing a material degree of hypercalcaemia (Hunter 1948) but carcinomatosis would not be entirely excluded by Snapper (1949) The plasma phosphorus is normal or only slightly increased and the alkaline phosphatase is normal The excretion of calcium in the

urine i increased Bence Jones protein is found in the urine in at least half the cases Geschickter and Copeland (1940) say it is present in 6 per cent Willis (1941) considers the finding of this protein should be regarded as evidence of extensive involvement of the marrow as it may be present with radiographic evidence entirely negative

Radiological appearances—The typical picture is that of multiple clear rounded lesions mostly the size of a pea or less but occasionally much larger even as large as an orange The lesions are endosteal the cortex being eroded from within the soft tissues may be invaded There is no sclerosis or periosteal reaction as a rule but a bone may be enlarged by the presence of multiple tumours Occasionally a lesion is grossly cystic and quite atypical as in a case with some ribs affected reported by Lichtenstein and Jaffe (1947) Kinney (1940) reported a case with gross cystic changes in the pelvis and upper femora what little bone there was left was crumpled up towards the end the patient could not be moved without the production of additional fractures in this case Bence-Jones protein could not be demonstrated in the urine Another case with marked cystic changes in some of the lesions was reported by Gill (1940) the serum calcium was 16 milligrams per 100 cubic centimetres but there was no hyperplasia of the parathyroids The typical skull with multiple fairly sharply cut holes is seen only in a proportion of the cases. Generalised osteoporosis may be the only skeletal change the appearance of the spine being suggestive of osteomalacia. Collapse of a vertebral body may occur

Progress—Death is the invariable result usually within eighteen months to two years. Just occasionally a case lives for several years. Remissions are seldom seen a remarkable remission of symptoms but with no change in the radiographs followed an attack of erysipelas (Irwin 1948) The kidneys are said to be damaged by the Bence Jones protein

Complications—Fractures recent or united were found in as many as 6_ per cent. of the cases by Geschickter and Copeland (1928) The ribs are particularly affected but fractures have also been seen in the clavicle and the sternum Amyloid deposit occurs in various organs in about 10 per cent of cases. A case showing myelomatosis and Paget s disease combined has been reported (Reich and Brodsky 1948)

Pathology—The tumours consist of masses of large cells with abundant cytoplasm often vacuolated and with nuclei containing one to four nucleoli The origin of the cells is not known with certainty and various types have been described mostly the cells appear to be plasma cells. Cases of the large cell type are said to be the ones with hyperglobulinaemia and rather often with Bence-Jones protein (Lichtenstein and Jaffe 1947) In the kidneys typical changes are found—tubular blockage with giant cells around the casts. The renal changes in eleven cases were studied by Bell (1933) The amyloid deposit in various organs either in nodular form or more diffuse differs in its distribution from that secondary to chronic suppuration. Instead of the usual sites of secondary amyloid in the liver spleen adrenals and kidneys the primary amyloidosis in multiple myeloma occurs in the smooth muscles of the gastro-intestinal and genito-urinary tracts and in the lungs heart tongue bones skin and nerves. It is also found in the joint capsules and is regarded as the cause of pain (Snapper 1940)

Diagnosis—Myelomatosis may have to be distinguished from a variety of conditions either by sternal or iliac puncture or by biopsy Carcinomatosis is not absolutely excluded by the presence of Bence-Jones protein which has been found also though only quite exceptionally in multiple sarcoma and a variety of other conditions (Geschickter and Copeland 1940) Conn (103) published a case of carcinomatosis of bronchial origin in which radiographs of the skull were extremely like myelomatosis. Metastases in the lungs practically rule out myelomatosis (Horsch 1935 Hodges *et al* 1941) Sclerosis around the skull lesions is in favour of carcinoma or sarcoma rather than myelomatosis (Horsch 1935) In Hand Schuller Christian disease the punched-out holes in the skull are generally more sharply cut less numerous and larger than those seen in myelomatosis. In the cases with generalised osteoporosis without local lesions osteomalacia and hyperparathyroidism have to be

considered The skull in a case of osteomalacia reported by Hunter (1931) was very like myelomatosis but the appearance completely changed as a result of appropriate treatment. Dr A Gilpin showed the present writer films of a case of lymphosarcoma in which the multiple lesions in many bones particularly the skull gave appearances indistinguishable from those seen in myelomatosis.

In *solitary myeloma or plasmacytoma* it is advisable to look carefully for other skeletal lesions. A case in which the myeloma is thought to be solitary will probably develop into myelomatosis eventually The solitary lesion may be regarded as the most innocent form of the disease and plasma-celled leukaemia, with the visceral organs infiltrated, as the most malignant (Tennent 1945) There is however no general agreement with this view Lumb (1948) reviewed the subject and reported a case with renal blockage similar to that found in multiple myeloma He added two more published cases of solitary myeloma to the twelve which were all that Willis (1941) regarded as adequately proved He stated that renal changes had been described in two of the published cases.

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CASE 181—MYELOMATOSIS

(Figs. 501 to 503.) L. V., male, aged fifty-one years. Pain in back with limitation of flexion for two years. Course of deep X-ray therapy. Blood examination revealed no anaemia. White cells 7,800. E.S.R. 48. Acid phosphatase 1.4 units. Alkaline phosphatase 8 units. No Bence Jones protein in urine. Radiographs showed suggestive clear spots in the skull, left fibula, right radius and both humeri and a large mass replacing the sacrum and adjacent parts of the ilia. Spine showed only generalised osteoporosis. Diagnosis confirmed by marrow puncture. Three years later man was still able to work. Radiographs showed considerable increase in size of the sacral tumour which had invaded the body of L. 5 vertebra. Lesion with collapse seen in D. 6 body and without collapse in C. 6 body. Skull lesions are decidedly larger. Humeri show a new spot or two but very little change. Lesions are also visible in both clavicles and scapulae, two ribs (one with fracture), left radius and possibly the ulna. Large lesion in lower third of left femur. (Under Mr. H. H. Langston.)



FIG. 501



FIG. 502

Case 181—Figure 501, skull in 1948 showing typical multiple lesions. Figure 502, skull in 1949 showing increase in size of several of the lesions. Note the destruction of the outer cortex by a large lesion at the vertex.



FIG. 503

Case 181—Pelvis in 1949 showing almost complete destruction of the sacrum and invasion of both ilia and the left half of L. 5 body.



FIG. 504
Case 181—Humerus 1948 showing a few typical circular lesions.



FIG. 505
Case 181—Femur in 1949 showing an osteolytic lesion distorting the cortex.

CASE 182—MYELOMATOSIS

(Figs 506 to 508) A. L female aged seventy nine years Bedridden for past three months with general asthenia and senility Eight weeks ago sustained a pathological fracture of right humerus. Radiographic examination revealed the nature of the case. Pain in the arm continued. On admission, angular deformity in right arm. Gross dorsal kyphosis. Very frail old woman. Bence Jones protein present in urine. Blood examination white cells 9 000 with polymorphonuclears 85 per cent Haemoglobin 62 per cent. Radiographs showed marked general osteoporosis with typical myelomatosis lesions in the skull pelvis and upper femora, humeri (fracture of right) clavicles scapulae and some ribs (with fractures) Some vertebral bodies collapsed apparently due in part to senile osteoporosis. The lesions in the humeri are far more numerous and striking than in other affected bones. Developed pneumonia and died a week after admission Post-mortem diagnosis confirmed by microscopic examination (Under Mr S A. Jenkins)



FIG 506
Case 182—Humeri showing typical lesions of myelomatosis in both, and fracture of the right.



Fig. 507
Case 1[illegible]—Skull showing [illegible] lesion [illegible] the [illegible]

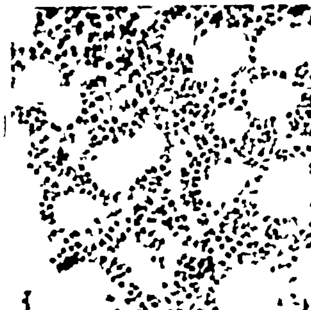


Fig. 508
Case 18[illegible]—Section of a lesion in humerus.

CASE 183—MYELOMATOSIS

(Fig. [illegible]) E. W. I. male aged forty-one years. Admitted with six months history of progressive weakness giddiness shortness of breath and attacks of buzzing in the head worse on exertion. Had lost 2 stone in weight. Treated for aplastic anaemia with blood transfusions. Spleen not enlarged. Blood examination red cell 1·06 million White cells 0 400 Haemoglobin 28 per cent. Later white cells fell to 4 000 to 1 000. Lymphocytes 4 per cent. Bence-Jones protein discovered in urine and radiographic examination showed typical myelomatosis in skull pelvis both femora (mostly in upper third) right scapula humerus and radius and several ribs. Renal function severely impaired. Blood pressure low. Considerable pain in legs. Died of uraemia fifteen months after occurrence of first symptoms. Post mortem diagnosis confirmed by examination of sternum and other bones. Parathyroids hypoplastic. Multiple white nodules in liver and kidneys which were much enlarged. Spleen not affected. (Under Dr Terence East.)



Fig. 509
Case 183—Skull showing exceptionally numerous typical lesions.

CHAPTER 62

NEUROBLASTOMA OF THE SUPRARENAL

Sympathico-blastoma

This is a malignant tumour usually of the adrenal medulla which metastasizes rapidly Cases are often divided into two clinical groups. In the Pepper type (1901) the liver is the chief site of metastases in Hutchison's syndrome (1907) the bones are specially invaded particularly the skull and the lower limbs. Not every case can be placed in one of these two groups. The tumour originates in primitive cells of the sympathetic nervous system usually but not invariably in one of the two adrenals which are equally prone to the disease At one time the Hutchison's syndrome was thought to be connected particularly with a tumour of the left suprarenal there was no support for this in the 138 cases studied by Scott et al (1933) In a few cases tumours have been found in both adrenals In some cases the tumour originates in the abdominal, thoracic pelvic or cervical sympathetic chain. Frew (1911) in his study of about thirty cases was convinced the growth spread by the lymphatics. This is not accepted as entirely true by Willis (1934) Both sexes are affected males rather more frequently Two or three years is the age of the majority according to Cockayne (194) but some authors maintain the average age is even lower particularly for the Pepper type. The tumour was congenital in five of Pepper's cases in one tumours were found in both adrenals. The cases with skeletal metastases are older than those without bone involvement

The symptoms are often misleading since they have no obvious connection with the primary growth and this even when suspected, often cannot be felt When the left gland is affected pain in the lower limbs and a limp the result of subperiosteal metastases are common early symptoms When the right adrenal is the seat of the neoplasm abdominal enlargement and pain may be complained of and the primary tumour is more likely to be felt on palpation glands may appear behind the right clavicle and right exophthalmos develops. In some cases a tumour presents on the back or the chest wall (Small 1940) An early sign may be haemorrhage into the upper eyelid—occasionally into both—followed by protrusion of the eyeball and these signs tend to occur first on the same side as the primary growth. Later both eyes are proptosed and optic atrophy may develop accompanied by headaches. *Swellings may appear on the skull particularly in the temporal fossa.* There is secondary anaemia attacks of fever and increasing cachexia particularly when the unusual number of bones invaded materially increases the possibility of haemorrhages occurring into some of the tumours. In addition to the osseous system and the liver metastases have been found in the kidneys lungs pancreas intestines ovary and brain (Stern and Newns 1937) In thirteen of the twenty-five new cases studied by these authors osseous metastases were present The bones most commonly affected are the skull ribs humeri tibiae femora and spine *Radiographs show diffuse mottling with clear spots in the affected portion of the skull* and separation of the sutures these changes may be secondary to a tumour in either suprarenal. In the long bones also there may be mottling the lesions being mostly osteolytic. In addition there may be smooth periosteal shadows occasionally a palisade arrangement of spicules on the surface like an osteogenic sarcoma has been seen. Good illustrations of both these changes were published by Stern and Newns The disease is fatal within a few months very few recoveries after early operation have been reported In a child of suitable age with haemorrhage into the eyelids and proptosis scurvy may have to be excluded In chloroma an even more uncommon condition than neuroblastoma the orbits and skull are often invaded and this must be excluded by examination of the blood

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CASE 184—METASTASES FROM NEUROBLASTOMA

(Fig 510) R D male aged two and a half years. When six months old a fall caused swelling in the left side of neck. Three months ago swelling recurred at same site and has steadily increased. Biopsy of gland thought to show inflammatory changes. On admission mass of glands in left side of neck fluctuant in places, and adherent to deeper structures. Chest consolidation of right base Glands increased in size Pathologist's report on section of gland neuroblastoma. Deep X-ray therapy without result Glands broke down and discharged haemorrhagic serous fluid. Swellings appeared in both the temporal regions and in the frontal. Discharge from left ear Developed bruising and oedema around both eyes and proptosis Abdominal examination negative Anaemia. White cells 2,600 Eosinophils 17 per cent Radiographs showed metastases in skull, with opening up of sutures and also in some ribs and the left femur Died nine weeks after admission. Post-mortem neuroblastoma of the left cervical region Metastases in kidneys and in the bones mentioned above. Thorax extensively invaded by the cervical growth. (Under Dr W P H Sheldon.)



FIG 510

Case 184—Skull showing multiple small metastases in the frontal and anterior portion of the parietal. Note the separation of th coronal suture.

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GLNLRAL INDEX